IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

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SHIRE DEVELOPMENT INC., SHIRE PHARMACEUTICAL DEVELOPMENT, INC., COSMO TECHNOLOGIES LIMITED, and GIULIANI INTERNATIONAL LIMITED,	:	CIVIL ACTION
Plaintiffs,	:	
v	:	
CADILA HEALTHCARE LIMITED (d/b/a ZYDUS CADIL) and ZYDUS PHARMACEUTICALS (USA) INC.,	:	
Defendants.	:	NO. 10-581-KAJ

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Wilmington, Delaware
Thursday, March 31, 2016
Bench Trial - Volume D

- - -

BEFORE: HONORABLE **KENT A. JORDAN**, U.S.C.C.J.

APPEARANCES:

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P R O C E E D I N G S

(REPORTER'S NOTE: The following bench trial was held in open court, beginning at 9:02 a.m.)

THE COURT: Good morning. Please be seated.

Mr. Gaertner.

MR. GAERTNER: Your Honor, before we call our next witness, you might recall Mr. Haug had mentioned earlier that we had an agreement where we stipulated to some of their exhibits regarding our ANDA and plaintiffs submitted to some of our exhibits regarding our NDA.

I'd like to now move into evidence our side of that stipulation, if we could.

THE COURT: All right.

MR. GAERTNER: So at this time, Your Honor, the defendants offer into evidence DTX-6, DTX-7, DTX-8, DTX-154, DTX-243, DTX-244, DTX-245, DTX-246, DTX-247, DTX-248, DTX-249, DTX-250, DTX-251, DTX-252, DTX-253, DTX-255, DTX-257, DTX-809, DTX-810, and DTX-852.

THE COURT: Thank you.

MR. HAUG: No objection.

THE COURT: It's admitted without objection.

(Above-referenced exhibits admitted into evidence.)

THE COURT: Your next witness then.

MR. ABRAMOWITZ: Good morning, your Honor. David Abramowitz.

Before we call the next witness, just one housekeeping matter. In looking at the exhibits that were admitted from Monday, it looks like we forgot to admit

Figure 2 of DTX-2009 which was used on cross of Dr. Pinal. We'd like to offer that into evidence.

MR. LIEF: I am not sure exactly what it is, but given our agreement about the figures and things, I guess no objection.

MR. ABRAMOWITZ: It's Figure 2 of the Vold article.

MR. LIEF: That's fine. No objection.

THE COURT: All right. It's admitted without objection.

(Figure 2 of DTX-2009 is admitted into evidence.)

MR. ABRAMOWITZ: Your Honor, we next call Dr. Thomas O'Halloran who conducted the melting point tests on the magnesium stearate.

THE COURT: All right.

.... THOMAS V. O'HALLORAN, having been first duly sworn, was examined and testified as follows ...

MR. ABRAMOWITZ: Your Honor, may I approach?

THE COURT: You may.

(Documents passed forward.)

DIRECT EXAMINATION

BY MR. ABRAMOWITZ:

Q. Good morning, Dr. O'Halloran.

A. Good morning.

Q. Can you please state your full name for the record?

A. My name is Thomas Vincent O'Halloran.

Q. And could you please state what your current position is?

A. I am currently the Charles E. and Emma H. Morrison Professor of Chemistry and Molecular Bioscience at Northwestern University.

I am also the Senior Advisor to the director of the Robert H. Lurie Comprehensive Cancer Center. And,

I am Founding Director of the Chemistry of Live Processes Institute at Northwestern.

Q. Can you briefly summarize for the Court your educational background after high school?

A. Yes. I attended the University of Missouri, Columbia, and obtained the Bachelor of Science Degree in Chemistry in 1979, and a Master's Degree in Chemistry in 1980.

I then went to Columbia University and obtained a Ph.D. in 1985.

Then I spent a year post-doctoral fellowship at Massachusetts Institute of Technology.

Q. Before you obtained your current position at Northwestern, could you briefly summarize your professional experience?

A. I stated in 1986 as an Assistant Professor at Northwestern in the Chemistry Department, and I was promoted

through the ranks to Associate Professor of Tenure, to Full Professor, which is my current position.

Q. Could you generally give the Court an idea about the focus of your academic research?

A. So my research follows three fundamental paths.

First of all, we synthesize and characterize metal organic compounds to use them as probes of biological function.

We also investigate metal complexes of proteins and other biomolecules to understand how metal responsive to switches work in biology. And,

Also, the third focus is ultrasensitive bio-analytical chemical methods to understand the biology of metal.

Q. Is magnesium stearate a salt, a metal salt, an organic compound?

A. Yes, it is.

Q. Can you turn to DTX-55 in your binder?

A. Okay.

Q. Is that a true and accurate copy of your CV up to the point it was provided? And does it detail your -- I'll leave it at is it a true and accurate copy?

A. Yes, it is an accurate copy with one minor change. I am no longer the Associate Director For Basic Science Research in the Robert H. Lurie Comprehensive Cancer Center.

I am now the Senior Advisor to the Director.

Q. Does it accurately reflect your academic professional experience and achievements?

A. Yes, with the exception of a couple more recent papers.

Q. Could you turn in your CV to page 12?

A. Yes.

Q. Looking at the papers listed as Nos. 60 and 61, is there something specifically important about those papers that you find relevant to this case?

A. These are some of the types of organic synthesis and characterization, novel compounds that involve metal organic compounds. And between these two papers, we published ten different melting points determined by the capillary melting point determination process. These papers have been cited over 400 times in the literature.

Q. Have you published other papers in peer-reviewed journals?

A. Yes.

Q. About how many?

A. Over 150, and they have appeared in some of the leading journals in the field of science: Nature Cell, Nature Chemical Biology, Journal of Controlled Drug Release, among others.

Q. Have you served as a reviewer for peer-reviewed

journals and grants?

A. Yes, I almost in a constant state of reviewing grants and other people's grants as well as journal articles.

Q. Turning to page 5 of your CV.

At the bottom, have you consulted any companies in the pharmaceutical and biological area?

A. Yes, ma'am. Yes, this is of great interest to me in the application of our academic findings. I have consulted at Eli Lilly, Hoffmann-La Roche, at Proctor and Gamble, Ciba Geigy, at that stage its name, Sandoz, Johnson Matthey, Wyeth, as well as several startup biotech companies that I am the co-founder of that are developing organic compounds and metal organic compounds to become pharmaceutical agents.

Q. With respect to your synthetic research, what's your history in using melting point as part of your research?

A. So this is one of the most fundamental methods that is taught in chemistry, taught to chemistry undergraduates. So since the late 70s, I have been using this as a method of characterization and used it throughout my career. I now supervise students and post-docs that use it.

Q. Dr. O'Halloran, do you have training in using melting point capillary apparatus such as oil baths?

A. Yes, I used a variety of instruments over my career, including the oil bath apparatus is that is typically used for a melting point determination.

MR. ABRAMOWITZ: Your Honor, defendants would offer DTX-55, Dr. O'Halloran's CV, into evidence.

MR. LIEF: No objection.

MR. ABRAMOWITZ: And defendants tender Dr. O'Halloran as an expert in analysis of metal organic compounds, including the determination of melting point through the capillary method.

MR. LIEF: No objection.

THE COURT: All right. Then the CV is admitted without objection. And I'll view the Doctor as an expert.

(DTX-55 is admitted into evidence.)

THE COURT: Go ahead.

BY MR. ABRAMOWITZ:

Q. Dr. O'Halloran, turn in your binder to Exhibit DTX-53.

A. (Witness complies.)

Q. Is that a true and accurate copy of a supplemental declaration reflecting testing that you provided in this case?

A. Yes, it is.

Q. Now, Dr. O'Halloran, could you please provide the Court sort of a brief description of what you were asked to do in this case?

A. I was approached by counsel to conduct a capillary melting point determination on a sample of magnesium stearate that they provided.

Q. Were you asked to give any opinion with respect to the melting point of the magnesium stearate in the context of claim 1 of the '720 patent?

A. No, I am not familiar with that patent.

Q. Did your laboratory conduct such a capillary melting point test?

A. Yes. I directed a senior post-doctoral research scientist in the laboratory to conduct this test.

Q. Before you carried out the test, did you review any documentation that was associated with the magnesium stearate sample?

A. Yes. So counsel provided me with the United States Pharmacopeia National Formulation Methods For Melting Point, 741. This is a standard laboratory methodology that would be accepted by the Court. And I reviewed that as well as the monograph on magnesium stearate. I inspected those and determined what the best process for determining capillary melting point range for this compound.

Q. Did the sample arrive to you with a certificate of analysis at any number indicating where the batch was from?

A. Yes. So the sample was delivered by counsel in a sealed container that bore the internal batch number 0908123024.

Q. Did the CFA indicate who the manufacturer of that particular sample was?

A. Yes. The manufacturer, as indicated, it was manufactured by Dr. Paul Lohmann and had a corresponding Dr. Paul Lohmann batch number of 1017233.

Q. And in formulating your efforts to test the magnesium stearate by capillary method, were you guided by any procedure in the USP?

A. Yes. The USP is written in a very general way to allow laboratories around the country using different apparatus to come to accurate measurements, and it defines those parameters.

The monograph instructs the investigator to determine the class of substance from the monograph on the compound. And when I looked through that, through the monograph of magnesium stearate, it listed no class.

MR. ABRAMOWITZ: Dylan, could you pull up Exhibit 3 of PTX-53.

BY MR. ABRAMOWITZ:

Q. Dr. O'Halloran, we're looking at the second supplement USP 37-NF 32 released June 31, 2014. Is this the USP NF supplement that you used to guide your testing procedures?

A. Yes, this is the most recent one. I also referred to the previous one in the development. And there is no substantial changes between this and the previous.

MR. ABRAMOWITZ: Could we go to page 6823 of the

second page of the exhibit, Dylan?

BY MR. ABRAMOWITZ:

Q. So looking at the second paragraph under the first title change to read, it is starts with "eight procedures."

Did this paragraph help guide you in determining how to take the melting point of magnesium stearate?

A. Yes. Since there was no class definition in the monograph of magnesium stearate, I proceeded to treat it as a class 1a substance as instructed in the monograph.

THE COURT: I've got to ask a question here. What did these classifications mean, Doctor? What does it mean for magnesium stearate to have no class? A representation of its manner? What does it mean?

THE WITNESS: So each class designation prescribes certain methods of handling and of investigating the substance. So the more unusual the characteristics or the more volatile, et cetera, then class definition then specifies in the definition in the USP how to handle that substance.

And so it's a gradated process, class 1a being the simplest kind of frequently white powders that don't really need special consideration.

THE COURT: Okay. So that has to do with safety concerns for people handling it?

THE WITNESS: As well as the chemical

properties. As the chemical properties become more difficult to handle at room temperature under an open flask, for instance, or if it's difficult to put into a tube, then it begins to have additional class definition characteristics. And it can go up to class 3 and class 4, get quite complex.

THE COURT: So it's about laboratory handling. It doesn't necessarily represent anything about what is pertinent to what is at issue in this case about melting point, or does it?

THE WITNESS: That's right. It's not pertinent. If there was a class 2 designation of the compound in the monograph, then deeper into this monograph, it says if it's a class 2 substance, you should flame-seal the capillary. It just gives some additional steps so that there can be reproducibility in the field.

THE COURT: Okay. Thank you.

Go ahead, Mr. Abramowitz.

MR. ABRAMOWITZ: Dylan, can we go to page 6824 and look at the procedure for class 1a?

BY MR. ABRAMOWITZ:

Q. Dr. O'Halloran, can you read the procedure for class 1a into the record?

A. Prepare the test substance and charge the capillary as directed in the procedure for class 1, apparatus I. Heat

the bath until the temperature is about 10 degrees below the expected melting point and is rising at a rate of about 1 degrees centigrade per minute. Insert the capillary as directed in the procedure for class 1, apparatus I when the temperature is about 5 degrees below the lower limit of the expected melting range, and continue heating until the melting is complete. Record the melting range as directed in procedure for class 1, apparatus I.

MR. ABRAMOWITZ: And since it talks about the procedures for class 1, can we go up to the prior two paragraphs, Dylan.

BY MR. ABRAMOWITZ:

Q. Dr. O'Halloran, could you read those into the record, just so we in the what is going on with class 1?

A. So, to reduce the substance under test to a very fine powder, and unless directed otherwise, render it anhydrous when it contains water of hydration by drying it at the temperature specified in the monograph, or when the substance contains no water of hydration, dry it over a suitable desiccant for no longer than 16 hours (or at the conditions stated in loss of drying, if appropriate).

Would you like me to read further?

Q. Yes. Can you continue on how you prepare the sample for testing?

A. And read this? Okay.

Charge a capillary glass tube, one end of which is sealed, with a sufficient amount of the dry powder to form a column in the bottom of the tube, 3 millimeters in height when packed down as closely as possible by moderate tapping on a solid surface. Due to the instrument design, alternative samples sizes may be instructed by the instrument manufacturer.

THE COURT: So I have another question, then, Doctor.

Given that first paragraph, does that mean that by definition, when you perform this procedure, you're going to be melting an anhydrous version of the magnesium stearate?

THE WITNESS: Sometimes the hydration state of the sample is not known, and so the monographs instruct you to inspect the compound's characteristics as described in the monograph -- this would be the monograph for magnesium stearate -- and then proceed according to instruction.

In the case of magnesium stearate, it does not indicate any waters of hydration; and so under that condition, you would proceed as a class 1a substance and dry it over desiccant.

THE COURT: Okay. Let me try to be more specific. Have you been here through the testimony of the witnesses.

THE WITNESS: For a few of them, but not all.

THE COURT: All right. I don't think I have given away anything about my thinking when I observed that there has been a lot of back and forth about whether the hydrated version of magnesium stearate melts or is merely dehydrated at a lower temperature at or around 88, 89, sub-90 degrees centigrade, but everybody agrees there is a melt of the hydrated version at some higher temperature. So the real fight here, hours and hours of fight, much labor has been invested in whether you describe what is happening at that lower temperature is a melt or not.

My question to you is simply, when this document tells you this is the procedure for testing whether or doing some kind of a melt test, it seems to say at the very outset that you should render the powder anhydrous. So what I am asking you is, someone following this procedure, by definition, do they end up testing the melt of the anhydrous version and not ever asking the question of whether the hydrated version melts or not? Do you understand?

THE WITNESS: Yes, I understand your question.

It turns out you can't always know the hydration state of the sample without a lot of additional experiments. And sometimes even heating at a certain temperature does not render the release of all the water in the sample. There are many different types of water of hydration.

So when I was asked, I was not asked to opine on any of these things. In fact, I did not know whether or not there was any water hydration. I was asked to take the substance as it was provided and make a measurement on it using the class. And I determined that it should be a class 1a definition, and I dried it for 16 hours over a desiccant.

So that is the procedure that I followed. And I am pretty confident that the material as I heard yesterday was it could have been hydrated, but I actually have no evidence of that, and I was not asked to opine on it.

THE COURT: All right. Thank you, Doctor.

MR. ABRAMOWITZ: Your Honor, maybe I can help clarify your point.

BY MR. ABRAMOWITZ:

Q. In drying the sample for your test, did you heat it at all?

A. No, I used the recommendation to dry it over a suitable desiccant for no longer than, no less than -- I am sorry, NLT is no less than -- 16 hours, and that is by the instruction in the monograph.

Q. And is that at room temperature?

A. That was desiccation at room temperature.

And so the desiccant, Your Honor, is a calcium sulfate that is a very dry material. It sits in the bottom of the glass container which is sealed and any types of

moisture or loosely bound waters of hydration are typically removed by that 16 hours in a desiccant.

THE COURT: Well, when you use a desiccant as opposed to heat to remove water, is the end result through either of those routes that you end up with anhydrous magnesium stearate?

THE WITNESS: It depends on the sample. And I do not have the expertise in, and I have not studied the literature on magnesium stearate to say to which degree it would be completely removed. And I think that is what a lot of the other experts were brought to opine on.

And so I actually did not know the hydration state. And I have no opinion on what, how many waters, how tightly bound they were. All I can tell you is that I've determined this fundamental kind of the most basic class of test on when a compound turns to liquid state from a solid. And I have done that on the compound that was described here.

THE COURT: Okay. Thanks.

Mr. Abramowitz.

MR. ABRAMOWITZ: Why don't we just turn to 6823, the paragraph entitled Apparatus.

BY MR. ABRAMOWITZ:

Q. Now, Dr. O'Halloran, did you use a specific melting point apparatus to carry out your test?

A. Yes. So I looked at both these options and I decided, knowing that there was controversy over the melting point, that I should observe, you know, I should instruct the post-doctoral research scientists to observe each temperature change of the status of the sample. So I chose a manual approach as opposed to an automated approach described under Apparatus II.

Apparatus I describes a fully manual process. I won't read it, but it has an oil bath, and it can have a controlled source of heat that is determined through an electronic current flow with a thermistor that will register the temperature. So it gives some automation. That is actually part of the description of Apparatus II.

I elected to use the Buchi B-540 which has characteristics that are directly in between Apparatus I and Apparatus II. In other words, it does not have an automated light beam interrogation of the sample and just prints out your melting point range. It gives the investigator a full control observation. But it does have a heating block instead of an oil bath. So that is why it's kind of in between the two definitions.

Q. Could you explain the mechanical characteristics of the Buchi B-540?

A. So Buchi B-540 is a small benchtop apparatus that has a large magnifying glass so that one can see these 1

millimeter capillary tubes in great detail.

It has a metal block inside and a ceramic cover and has three holes that allow insertion of three capillaries, so three substances can be observed simultaneously in it.

Then has an LED on the front or a display that gives the current temperature. And then it also has programmable ramps so the heating can be applied through an electronic process in a stepwise manner.

Q. Can you actually describe how the test was carried out?

A. So I instructed the post-doctoral research associate to break the seal on the sample that was provided by counsel and transfer some of it into a separate vial into the desiccator, and it was there for over 16 hours when he removed it and then filled a capillary to a level of three millimeters, tapping it down, and using the prescribed method in the 741 monograph.

He then placed the capillary along with two standards, vanillin and phenacetic acid. These are USP standards that are certified to melt in a very specific range.

And he filled those the same way and inserted them into each other within the melting point apparatus. It was preheated to a temperature of 70 degrees. And while the

monograph says to go to 10 degrees before the melting point, and then slow down the rate of heating to one degree centigrade per minute, we took the cautious approach of just heating one degree per minute throughout the entire range from 70 degrees to past the full melting point.

Q. Did you give any instructions to your post-doctoral scientists about how to record the results of the experiment?

A. Yes, I asked them to continuously observe the sample and to record any types of physical changes that he observed in the sample or within the capillary, to note any droplets of water or anything that he would see that are relevant.

Q. And were you personally present during the experiment?

A. Yes, I was there at the beginning and the setup and for the first half hour, and then I left, and I came back when the temperature was getting close to the anticipated melting range. And so I observed with him and watched him record in his notebook.

Q. What were the results for the experimental samples in the standards?

A. So the experimental samples showed no physical change until a temperature of 139.7 degrees. And then we observed a kind of a collapse in the height of the sample. We call that "solid shrink." It shrank about 20 or 30 percent, but

it did not show any sign of liquid. So by the monograph, we did not record that as the beginning or the onset of the melting.

Then a few degrees later, at 143 degrees, we see a liquid and solid mixture.

Then the monograph instructs us to note the temperature where the sample is first seen to be completely liquid. And that is 145.5 degrees.

Q. And where is the standard melt?

A. So one of the standards was vanillin, and its melting temperature that we observed was 81.5 degrees to 82.8. So that was its melting point range that we observed.

The United States Pharmacopeia standards indicate that the melting point should be between 81 and 83. So that standard did exactly what we expected if the instrument was working.

We then observed the melting point of the second standard that was phenacetin, and it melted at 135 to 136.1 degrees. So from the beginning of liquid appearance until it was fully liquid.

By the USP standards, the acceptable range is 134 to 136.6. So these standards have about a two degree, three degree melting point range.

Q. What do the melting point standards tell you?

A. The fact that both of these standards melted as

according to what was described as the behavior of the standard material, this indicated that the Buchi B-540 was operating properly.

Q. And are the relevant findings from the laboratory notebook where these observations were recorded presented in Exhibit 9 of your declaration, DTX-53?

A. Yes, the details from the samples delivery and the handling of the sample through the end of the experiment are all detailed there.

MR. ABRAMOWITZ: Your Honor, we would offer Exhibit 9 of DTX-53 into evidence.

MR. LIEF: No objection.

THE COURT: It's admitted without objection.

(Exhibit 9 of DTX-53 is admitted into evidence.)

MR. ABRAMOWITZ: I just want to clarify for the record that to make sure that everybody is on the same page here.

BY MR. ABRAMOWITZ:

Q. Dr. O'Halloran, did you consider or opine any DSC testing in Zydus's ANDA product?

THE COURT: I am sorry. You need to say that again a little bit more slowly.

BY MR. ABRAMOWITZ:

Q. Dr. O'Halloran, were you asked to consider or opine any DSC testing?

A. No, I wasn't.
Q. Were you asked to consider or opine on any TGA testing?
A. No, I wasn't.
Q. Were you asked to consider or opine any hot stage testing?
A. No, I was not.
Q. Were you asked to consider or opine on the opinions or expert reports in your depositions of any other expert in your case?
A. No, I did not see them.
Q. Were you asked to consider or opine whether magnesium stearate exists in a hydrated compound?
A. No, I was not.
Q. Were you asked to opine or consider any of the peer reviewed literature or treatises that describe the melting point of magnesium stearate?
A. No, I was not.

MR. ABRAMOWITZ: Your Honor, we have no further questions of Dr. O'Halloran.

THE COURT: Cross-examination, Mr. Lief.

CROSS-EXAMINATION

BY MR. LIEF:
Q. Good morning, Dr. O'Halloran.
A. Good morning.

Q. Dr. O'Halloran, am I correct that you have never worked --

MR. GEORGEK: May I hand this up?

MR. LIEF: Oh. May we hand this up?

THE COURT: Yes, you can freely approach the witness.

(Binders passed forward.)

BY MR. LIEF:

Q. Dr. O'Halloran, am I correct that you have never worked with magnesium stearate before this case?

A. Correct.

Q. With respect to the sample that you received from counsel, am I correct that before anything was done to it, you have no idea, one way or the other, whether that sample was hydrated or anhydrous; correct?

A. That is correct.

Q. Am I also correct that in the past, you have determined whether various materials were hydrated or anhydrous by using testing?

A. By using?

Q. Testing.

A. Testing, yes.

Q. And you know how to do that; correct?

A. Correct.

Q. But none of that type of testing was done here;

correct?

A. Correct.

Q. Now, after you received the sample from counsel, I believe as you testified on direct, you did place it in an desiccator for 16 hours pursuant to the procedure we saw; correct?

A. Exactly, that's correct.

Q. When the sample then came out of that desiccator, am I correct that you have no idea whether that sample that came out of the desiccator was hydrated or anhydrous?

A. That is correct.

Q. And, again, you did no testing on that material to determine that; correct?

A. Correct. For a class 1a substance, that is not specified any longer.

Q. Okay. And if I heard you correctly, you didn't look at the patent in this case?

A. That is correct.

Q. And you didn't look at any literature on magnesium stearate either?

A. That's correct.

Q. And so you didn't take any of that into account in determining what test you should do; correct?

A. That is correct.

Q. Okay. And so to summarize, with respect to the

material that you actually tested and put into the melting point capillary equipment, you simply don't know, one way or another, whether it was anhydrous; correct?

A. That's correct. I can only tell you my observation that the material looked identical in and out of the desiccator. That is a clear vessel, and it freely flowed, so it did not take on obvious signs of hydration -- or changes in hydration.

Q. And, Dr. O'Halloran, were you here in court when Dr. Sacchetti testified?

A. No. Dr. Sacchetti is from what institution?

THE COURT: Wisconsin.

THE WITNESS: Wisconsin.

BY THE WITNESS:

A. Yes, I was there for that, for the plate melt.

Q. The plate melt?

A. Yes.

Q. And did you hear him testify about in his view some digital evidence of melting at 130?

A. Yes.

Q. Now, I take it, this capillary tube thing is a visual method of its own?

A. That is correct.

Q. Your visual method, you found the melting point of, what was it, 145?

A. It was 143 to 145 point something.
Q. And do you find it curious that these two different visual methods gave numbers some 13 degrees apart from each other?
A. So I wish I knew I could tell you that I have done the hot plate melting determination with the microscope, but I have not, so I am just not familiar with how samples might differ between that method and the capillary melting point determination.

I did note there was a solid shrink, so there is some phase change or something going on that. I don't know what the chemical nature of that is. Remember, I mentioned that at 139.

Q. At 139, you saw something?
A. The solid shrink, yes.
Q. But not at 130?
A. Not at 130.
Q. Right. Now, in your experience in chemistry, is it possible for a liquid to form without it being visible?
A. For a liquid to form. If the droplet is below the size of some X microns, then you wouldn't see a droplet of liquid. That's possible.
Q. And so that is conceivable that at the very earliest stage of a phase change, you wouldn't be able to see the liquid. That is conceivable; correct?

A. That is correct.

MR. LIEF: Thank you. No further questions.

THE COURT: Any redirect?

MR. ABRAMOWITZ: No.

THE COURT: All right. Thank you, Doctor.

THE WITNESS: Thank you. Do I take these?

THE COURT: Yes, that would probably be helpful. Thanks very much.

MS. WAYDA: Good morning, Your Honor.

THE COURT: Good morning.

MS. WAYDA: Andrea Wayda for Zydus.

Zydus calls as its next witness, Dr. Joseph A. Gardella, Jr. to provide his opinions on Dr. Davies' Raman color mapping and optical microscopy of the cross-sections of the Zydus ANDA product.

Your Honor, may we approach the bench and the witness to deliver the materials?

THE COURT: You may.

(Documents passed forward.)

... JOSEPH A. GARDELLA, JR., having been first duly sworn, was examined and testified as follows ...

MS. WAYDA: May I proceed, Your Honor?

THE COURT: You may, please.

DIRECT EXAMINATION

BY MS. WAYDA:

Q. Good morning, Dr. Gardella. Can you state your name and address for the record?

A. Yes. My name is Joseph A. Gardella, Jr. And I live at 178 Admiral Road in Buffalo, New York.

Q. What is your profession?

A. I am a professor and a researcher in pharmaceutical sciences, materials, chemistry with patents and publications in fields, relevant fields like controlled release and drug delivery.

Q. Did you prepare a list of demonstratives or a slide deck to assist you in providing your testimony today?

A. Yes, I did.

MS. WAYDA: Your Honor, you will find the slide deck in your notebook. And,

Mr. Green, if you can put up the second slide.

BY MS. WAYDA:

Q. Dr. Gardella, I am showing you DDX-7.2. Using this, can you please describe your educational background?

A. Yes. As shown on the slide DDX-7.2, I received a Bachelor's Degree in Chemistry and a Bachelor's Degree in Philosophy from Oakland University in 1977.

I then continued for a Ph.D. in Analytical Chemistry from the University of Pittsburgh with David Hercules that was awarded in 1981.

I then left to go to Utah to do a post-doctoral

research fellowship in the area of Vibrational Spectroscopy with Edward Irene at the Chemistry Department of Utah from '81 to '82.

Q. Could you also briefly describe your professional experiences since obtaining your PhD?

A. Yes. Following my post-doctoral stint, I was appointed as a faculty member in the Department of Chemistry in the University of Buffalo, State University in New York, where I moved up through the ranks and then was promoted finally to my current position as a State University of New York Distinguished Professor of Chemistry. And I hold the John and Frances Larkin Endowed Professor of Chemistry.

Over that period, I have published somewhere more than 250 peer-reviewed publications in the fields that are shown here, including controlled release and drug delivery, tissue engineering, mapping, and the details of quantitative details of mapping, chemical analysis.

Q. Using DDX-7.3, can you please describe for the Court your qualifications and specialties in the pharmaceutical sciences that are relevant to this case?

A. Certainly. As shown on this slide, No. 3, I have especially over the last two years worked in experimental chemical mapping by a variety of techniques, including Raman spectroscopy. And I have special expertise during that period in the details of statistical analysis of the data

and numerous publications in pharmaceutical and chemical data analysis and imaging and mapping analysis.

Further, over the last 33 years, I have been teaching basic introductory and advanced statistics and analytical methodology to students; in particular, of relevance here to pre-pharmacy and Pharm.D program students at the University of Buffalo.

Q. Can you please turn to your binder and look with me at DTX-119?

A. (Witness complies.)

Q. Do you recognize this document?

A. Yes. This is my CV as of June 2014.

Q. And is the information contained in your curriculum vitae accurate and up-to-date?

A. Up-to-date to that point in June of 2014, yes.

Q. Could you please describe for us the changes to your CV since June 2014?

A. Yes. Over the nearly two years, I have published more papers and added additional students to my research group. I have given more talks, all of them just routine yearly progress, taught more courses.

MS. WAYDA: Your Honor, at this time we offer DTX-119 into evidence.

MR. HAUG: No objection.

THE COURT: Admitted without objection.

(DTX-119 is admitted into evidence.)

BY MS. WAYDA:

Q. Dr. Gardella, have you previously acted as an expert in the area of pharmaceutical sciences?

A. Yes. Over the last 17 years, I have served as an expert in pharmaceutical work in about 10 different projects or matters.

Q. And in those matters, have you been accepted by the Court as an expert?

A. Yes. I've been accepted by the Court as an expert in cases in the United States and in England; and then served as an expert in pharmaceutical cases in medical products cases in Canada, Sweden, and Germany.

MS. WAYDA: At this time, Your Honor, we offer Dr. Gardella as an expert in the area of quantitative and qualitative analysis of materials, including pharmaceutical formulations using a variety of mass, electron, and vibrational spectroscopy techniques, including Raman spectroscopy.

MR. HAUG: No objection.

THE COURT: He is here an expert. Go ahead.

MS. WAYDA: Thank you, Your Honor.

BY MS. WAYDA:

Q. Dr. Gardella, using DDX-7.4, can you please explain to the Court what your understanding is what you have been

asked to do in this case?

A. Yes. I was asked to review and analyze, as shown here in data, both the optical microscopy results and the Raman mapping studies performed by Dr. Davies on the Zydus ANDA product. And,

Secondly, I was asked to determine if Dr. Davies' Raman mapping studies supported Dr. Sinko's reference to those data and reliance on his Raman data in support of his opinion that the Zydus ANDA product contains mesalamine "dispersed -- this is in quotes -- "dispersed both in a lipophilic matrix and in a hydrophilic matrix."

Q. Turning to the next slide, DDX-7.5.

Would you please give a high level summary to the Court of what you have concluded from your work?

A. Sure. Dr. Davies' Raman maps simply show mesalamine distributed throughout the Zydus ANDA product, and they provide no information on how much mesalamine is present in any particular area. And,

In summary, the Raman data really provide no basis for Dr. Sinko to refer to them and rely on that in support of his conclusion as stated previously.

And the optical micrographs provide no data regarding whether or not the mesalamine or excipients in the Zydus ANDA product are located in any matrix at all. They provide no information on the identity or properties of any

material located in any "particles" or "granules."

Q. Dr. Gardella, I think it would be helpful to the Court if you could walk through what you did in analyzing your Raman mapping data or Dr. Davies' Raman mapping data in order to reach those conclusions. And I believe you prepared a slide --

A. Sure.

Q. -- on 7.6.

THE COURT: Hold on just a second. Just for the sake of our court reporters, even though in ordinary conversation, it is normal for people to sort of speak over one another, you have to wait for the question to finish before you start answering, and you have to wait for his answer to finish before you start asking your next question. Okay?

THE WITNESS: I apologize.

THE COURT: That's fine.

All right. Go ahead, please.

THE WITNESS: Sure.

BY THE WITNESS:

A. As shown on this next demonstrative is a summary of the procedure that I undertook. So first I would say that counsel obtained a copy of the software that operates the Raman microscope that Dr. Davies used, and so that I -- and Dr. Davies had provided the underlying digital data, and so

I could open his digital files and relate those to the things in his report. He did not provide in his report a procedure of how he analyzed the data, so I used the standard procedure that I have laid out here in these steps. If I could just walk through them, Your Honor.

So the first thing I did, because Dr. Davies didn't collect any data in his digital files of the Raman spectra of authentic excipients in the Zydus AND product, I found Raman -- I researched and documented in my report sources of reference, Raman spectra of excipients in particular, looking for measurements made by the same instrumentation that Dr. Davies used because of a sensitivity to certain factors in Raman spectroscopy.

For magnesium stearate, silicon dioxide, microcrystalline cellulose, carboxymethylcellulose, sodium -- hydroxypropylmethylcellulose, and sodium starch glycolate. Those, as I understood and reported in my report, are those used in the Zydus ANDA product.

Q. Now, let me stop you here, Dr. Gardella. Why was it important for you to obtain reference spectra of those excipients?

A. Well, there is a couple of reasons that I have laid out here. There was no discussion of any excipients except some discussion about the excipients and their fluorescence in Dr. Davies' reports, and he didn't lay out a procedure of

how he -- and all I had was his report. There was no details about the procedures.

So these are just the standard approaches when you are analyzing a commercial pharmaceutical product in my experience is to gather all the information about authentic material as you can. And,

No. 2 then, the first thing I wanted to ask is to make sure is that none of the signals, the peaks from the excipients would interfere with the region that Dr. Davies used to integrate a peak that then was transformed in the color coding of the maps.

THE COURT: Hold on just a moment, if you would.

What do you mean, Doctor, when you say "integrate a peak?"

THE WITNESS: So as Dr. Davies discussed in his testimony that was shown here, there was a peak in the reference spectra of mesalamine that he recorded in his report, and it was in the digital files at 817 wave numbers is the unit in the spectrum.

And he integrated, summed up all the signals together. He didn't just use the signal at the top of the peak. It is a standard procedure.

THE COURT: So you are saying integration of the map matters.

THE WITNESS: Exactly.

THE COURT: All right. Thanks. Go ahead.

THE WITNESS: So that was what was actually used, and the only thing that was used to make these color maps.

BY MS. WAYDA:

Q. Dr. Gardella, if I may stop you there. When I look at that map, and perhaps the Court is as well, I see what seems to be a lot of structure in that map. Could you please explain to us what we're looking at when we see that map?

A. Sure. This is just simply a ranking of the integrated intensity on a thermal, what is called a thermal color scale that ranges from black to white and going through orange and brown and yellow. It's a very standard way to rank different intensities in a way that is commonly used to visual recognition.

So it was my job to really, not knowing anything about what the maps were in his report other than the mesalamine is to really interrogate the underlying digital data and try to understand, first, how the maps were created and, secondly, what they meant.

Q. Okay. Can you continue with your third point on DDX-7.6?

A. So once I determined from No. 2 that none of the excipients had peaks, strong peaks that would interfere with

that choice of a peak that Dr. Davies and his staff used to create the maps, I then identified in my report the strongest peaks characteristic of each excipient so that if I, in interrogating the underlying data, found evidence of detection of the excipients, I could have created individual maps of each of the excipients in a manner similar to what Dr. Davies did for mesalamine and overlaid them to show if there was any spacial distribution of each excipient relative to each other and to mesalamine.

Q. Please continue.

A. And I then interrogated both, as described in my report, both the average overall spectrum for the entire area that was mapped and used the data analysis to examine spectra in individual parts down to the level of individual pixels.

Dr. Davies testified in his deposition that he examined the individual pixels, values for the individual pixels in the same way. I did it by looking at the individual spectra.

Q. Dr. Gardella, let me ask you, why is it important in your mind to look at each individual pixel?

A. Well, as you noted, if you examine these maps, there is a suggestion of different regions because of the different colors, especially the black color, and so I just really wanted to look.

In Dr. Davies report, he also reported the black color included fluorescence which, in his report, he said related to some unspecified excipient. So I just wanted to look at those individual reasons to see what the difference was between brown areas, black areas, yellow areas, white areas, and see how the individual spectra -- you know, if there was any evidence perhaps in, for example, if there was an area that was black and had fluorescence, was there any evidence of an excipient in that area? Dr. Davies didn't discuss those kinds of steps. So I was just doing what I would do in analyzing the data.

Q. And to be clear, Dr. Davies included no information on how he analyzed his Raman maps in his report; correct?

A. The only thing that was stated is that he integrated -- he and his staff integrated the individual, that range from 795 to 835, and that integrated area was used to create the maps.

Q. And please continue with point 5 on DDX-7.6.

A. In the black areas then, I was particularly concerned with deciding -- since Dr. Davies had reported on the presence throughout; there is, in analytical chemistry, we establish, especially in regulatory situations, we establish criteria using illuminative detection to tell us whether something is present or whether it is not detected; so I wanted to do that, look at the peak of interest to see what the black

colors meant and what was the minimum color value. And then I constructed color coded maps which represent the distribution of mesalamine across the cross section of the Zydus ANDA product in the same way.

Q. To be clear, PTX-902 in the left side of DDX-7.6, what is shown there?

A. This is simply a map of that intensity, integrated of only that peak, and represents the presence of mesalamine throughout the area that is mapped.

Q. Turning to your next slide, DDX-7.7. Can you please summarize for the Court what you concluded from your review of Dr. Davies' native data files and Dr. Davies' Raman mapping studies?

A. Yes, the Raman data only shows that mesalamine is distributed throughout the Zydus ANDA product. And I want to be clear that his data provides no information on how much mesalamine is present in any one area. And,

Secondly --

Q. But --

A. -- this really -- sorry.

Q. Let me stop you there. There is different colors. Why wouldn't that tell you a brighter color is more mesalamine and a lighter color or a darker color is less mesalamine?

A. Sure. In my report, I discussed from peer-reviewed

papers the standard procedures about what you need to do to turn those intensities into concentrations. That wasn't done, and there was really no information available to do it from the experimental data that was provided.

THE COURT: Pardon me for interrupting. Is there a correlation? Is there a meaningful inference that can be drawn by looking at the variations in the color intensity and understanding something about the concentration of mesalamine associated with that?

THE WITNESS: No, not by the strict rules we have to go by in this. Raman spectroscopy is not a really simple technique that has a quantitative relationship simply between the intensity and the concentration. There are other reasons discussed in my report as to why a slight variation in intensity could be due to roughness of the surface or other things that affect the scattering process. So it's unlike other sort of spectroscopic techniques where there is really a straightforward relationship between intensity that it is well known and you can then imply. You know, in Raman mapping, that is not the case. Careful calibration has to be done.

THE COURT: All right. Thank you. Go ahead.

THE WITNESS: And I should say, if I could, Your Honor that Dr. Davies never, in either of his depositions or his report, implied that there was anything other than the

presence throughout.

THE COURT: All right. Thank you.

BY MS. WAYDA:

Q. Dr. Gardella, if you can continue with the second point on DDX-7.7.

A. Yes. Just in what I understood about what Dr. Sinko -- was told to me about what Dr. Sinko offered as an opinion, I don't believe there is any basis for him to rely on Dr. Davies' Raman data in support of his opinion that the Zydus ANDA product contains mesalamine dispersed both in a lipophilic matrix and a hydrophilic matrix.

Q. Let's turn to the next slide and try to unpack each of these opinions. What is the basis for the first conclusion that you gave that is on DDX-7.7? And please use DDX-7.8.

A. Yes. Thank you. Just this follows a bit from Your Honor's question.

The Raman images contained in his reports and in the digital data did not have any intensity scale associated with them. So I really didn't understand, nor could I understand without interrogating visually all the pixels, what the difference was between the dark areas and the bright areas in terms of the signal intensity.

Usually you have a color bar associated with it, and he, in his testimony that was played here on Monday, he

had a figure that, for the first time, had a color bar associated with it.

The units on the color bar are from 0 to 5,000 and labeled as AU, which stands for arbitrary units. And so there is no way of knowing how much mesalamine corresponds to the color selected or if the distribution is homogeneous.

MS. WAYDA: Mr. Green, can you please put up PTX-902.

BY MS. WAYDA:

Q. Dr. Gardella, is this what you were referring to as the original image as received in Dr. Davies' expert report?

A. Yes, it is. So as you can see, there is a scale bar on it that tells you the size that is represented, but there is no scale for the color which is normally provided when you do this kind of mapping.

Q. Now, Dr. Gardella, you used a term in your testimony "arbitrary units." What do you mean by arbitrary units?

A. Usually we use the term "arbitrary units" to represent that we have not done a calibration that changes the signal intensity to a concentration. And so in this case, the arbitrary units, I have investigated by looking into the original data. The 0 to 5,000 represents the value of the integrated signal that ranged from 0 to 5,000. So we call that arbitrary units because if you change some of the characteristics of the instrumentation, you may get the same

map, but it may just range with a signal intensity from 0 to 200. So it represents the same change in distribution but it is an arbitrary unit until it is transformed into a concentration.

Q. Dr. Gardella, looking now at DDX-7.9, can you use that demonstrative to provide an explanation to the Court about your opinion regarding Dr. Sinko's use of the mesalamine and the inner lipophilic and outer hydrophilic matrices?

A. So I will just summarize my conclusions.

None of the excipients in the Zydus ANDA product could be detected in the Raman maps.

And Dr. Davies' Raman maps demonstrate the presence of mesalamine, but there is no evidence to show where that mesalamine is located with respect to any excipients in the Zydus ANDA product.

And no matrices or structures of excipients can be determined from the Raman data or maps; simply differences in brightness are due only to the different intensities of the mesalamine peak.

Q. Now, to be clear, Dr. Gardella, neither you nor Dr. Davies gave any discussion in your expert reports?

THE COURT: Let me interrupt. I apologize.

MS. WAYDA: I am sorry, Your Honor.

THE COURT: I missed the last thing you said.

Can you repeat the last thing you said?

THE WITNESS: Certainly. I'll repeat the entire thing.

No matrices or structures of excipients can be determined from the Raman data or the maps. So the underlying Raman data, the individual spectra, point by point spectra or the maps. So the differences in brightness that you see are due only to different intensities of the mesalamine peak. That is all the information that is there.

THE COURT: Okay. What does that mean, "differences in brightness are due only to the different intensities of the mesalamine peak?" What does that mean?

THE WITNESS: So I'll start to say that it is really literal. There is nothing implied in it. There are differences in brightness that we see in the brightness scale, and they're only due to different intensities -- intensities, not concentrations, just the intensities of the mesalamine peak.

THE COURT: And what does the intensity relate to? If it does not relate to concentration, does it relate to anything?

THE WITNESS: Yes.

THE COURT: Or is it just arbitrary?

THE WITNESS: No, certainly concentration is important in the changing intensity, but so is the

scattering process itself which leads to intensity changes in Raman. And so if, and in my report, I talked about this in particular about all the factors you have to control in Raman mapping to change it.

So, for example, the most common thing is that the scattering changes because you are at a different roughness on the surface and you get less scattering even though you have exactly the same amount of mesalamine in it.

THE COURT: When you said that if there were a scale provided, then you would know something about concentration. Did I hear that right?

THE WITNESS: That's right. If a scale had been provided that took into account all of these factors, then you -- so there was no scale, and I wanted to know was there any processing? Dr. Davies didn't tell us whether there were any processing steps. Was there any processing to change that intensity into a concentration or a rough estimate of concentration, or there are treatments you can do in that software that take advantage of how smooth is the surface and you can do those things. There was nothing but the intensity of the integrated peak as shown by Dr. Davies when he gave his testimony, when it was filmed. I was present for that.

THE COURT: Okay. Thank you.

MS. WAYDA: Your Honor, if I may follow-up on

your question and ask.

BY MS. WAYDA:

Q. Dr. Gardella, is it possible to quantitate a Raman color map?

A. Yes.

Q. Could you please briefly describe how that would be done?

A. Sure. I described this in my report by referring to an article by Gordon. And what you would have to do is run standards using all of the components that are present. You'd have to make synthetic standards with different amounts of mesalamine and then measure that intensity in the presence of the other excipients and make a calibration curve essentially, is what we called it in analytical chemistry, in order to then change that intensity into a concentration.

THE COURT: Okay. Thank you.

MS. WAYDA: Your Honor, I'd just like to follow-up on a question I was asking when I didn't notice that you wanted to ask a question. I apologize for that.

BY MS. WAYDA:

Q. But I want to make clear, Dr. Gardella, and Dr. Davies as well, you are not deriving your third opinion there based on anything on the pharmaceutical formulation of the Zydus ANDA product?

A. That is correct.
Q. Are you just basing it on the Raman data maps?
A. That is exactly right.
Q. Now, I'd like to turn now to the next series of opinions that you gave, and that was on the optical microscopy that Dr. Davies conducted on the cross-sections of the Zydus ANDA product. And I am going to ask you, did you review the optical images recorded by Dr. Davies?
A. Yes, there were six optical micrographs like this one using a particular microscope and then 914, I think, individual higher spacial resolution micrographs. And I examined all of them. Those were for the two samples that Dr. Davies analyzed, the EMH345 and EMM196.

I am showing here one of those again taken from Dr. Davies testimony and from his deposition. One of these, where he was asked to and labeled with a G. He circled or enclosed with a pen granules that the labeled with Gs, and then particles which are hard to see from here, particles he circled and labeled them P.

He labeled about 10 granules across this, and I don't know, maybe 10 things that he said were particles.
Q. To be clear, this information on labeling of granules and particles, was this included in Dr. Davies' expert report?
A. No.

Q. What, if anything, did you conclude based on your review of those optical images?

A. Dr. Davies, in his report, concluded that the Zydus ANDA product contained particles and/or granules and, as he did in his deposition and his testimony, just said they were particles and/or granules.

He started, I should say, by calling them features in general and then talked specifically about particles and granules. And the image really provides no additional information that would allow a conclusion that the Zydus ANDA product has any particular structures, matrices, lipophilic or hydrophilic matrices, because that would require information of other chemical composition of those structures, and there is no information from an optical micrograph about the chemical composition.

Q. And to be clear, Dr. Gardella, you are not offering an opinion in this case on what constitutes a lipophilic matrix or a hydrophilic matrix; correct?

A. No, I am not.

Q. You are basing your testimony there just solely on the fact that magnesium stearate is a known lipophile?

A. Well, that is correct.

Q. And that other materials such as CMC and sodium starch glycolate are hydrophilic materials?

MR. HAUG: Objection, leading.

THE COURT: Yes, sustained.

BY MS. WAYDA:

Q. Now, were you in the courtroom for Dr. Davies' testimony in which he equated an optical image of a granule which we marked as G1 -- and if we could put up PDX-2.11 -- with a Raman map that he said corresponded to the same area occupied by that granule labeled G1, and that was PDX-2.12. Do you recall that testimony?

A. Yes, I was present for the testimony.

Q. Does Dr. Davies' testimony regarding the Raman map and optical image for G1 changed any of your opinions in this case?

A. No, it does not.

Q. And why not?

A. Well, this was actually the very first time in his trial testimony that he provided information about the location of both the Raman maps and the digital optical images. And so I was able, after his testimony, to look at these two things to see if there was anything that could draw any conclusion between them. And there really was no information in the Raman maps other than the Raman data showed that the mesalamine is distributed throughout the entire sample. That means inside what he calls a granule and outside what he calls a granule.

MS. WAYDA: Mr. Green, if we could please put up

PDX-2.13 and then PDX-2.14.

BY MS. WAYDA:

Q. Would your testimony be the same with respect to the second granule that he identified in his trial testimony G2 which is shown in the optical microscope image in PDX-2.13 and the Raman map that he said is associated with G2 in PDX-2.14?

A. My opinion is exactly the same as I have stated it previously. This is the first time that I saw any correspondence between where the Raman maps were and where the optical micrographs were, but, again, all the comparison of these two show you is that mesalamine is distributed both inside what he identified as a granule and outside. And it is just present.

Q. Dr. Gardella, I believe you were also in the courtroom for Dr. Little's testimony, and I am going to refresh your recollection as to what he testified at trial transcript, page 214, lines 11 through 16 in response to a question about particles floating in the dissolution medium obtained by Dr. Gray:

"Answer: (Continuing) so what you get is the size scale just like we discussed in the deposition that is exactly what I would expect to see that would come through a .8-millimeter filter, which is in that first dry granulation stage, and is, in fact, exactly the same as the size of the

inner granules that you saw in Dr. Davies' results earlier."

Do you recall that testimony?

A. I do.

Q. Now, in Dr. Davies' optical microscopy data and in his expert report, did you see any evidence for "inner granules" of 0.8 millimeters in size?

A. All I saw were evidence, as Dr. Davies stated in his reports and his depositions and in his testimony, that there were particles and granules in the range from 10 microns to 500 microns distributed throughout. And I didn't see any correspondence between that conclusion and the size distribution that Dr. Little was talking about.

Q. There were how many optical images again that you looked at?

A. The sum total is a little bit over 920 of them.

Q. And we only had information from Dr. Davies on G1 and G2; is that correct?

A. That's correct.

Q. And did Dr. Davies conduct any particle size distribution analysis of the granules that he alleged that he saw in size between 10 and 500 microns?

A. Yes. As I had stated in my report, there was no evidence of any quantitative technique for determining the distribution of the sizes, meaning how many particles had a particular size, and he only gave a broad range and stated

that particles and granules were in them, and never separately said here is a range of sizes for granules, what I consider a granule. And he was asked this at I think both his depositions and said he just made the range for particles and granules.

Q. So there is no evidence in this record that there is anything more than G1 and G2 that corresponds to these alleged .8 millimeter size granules that Dr. Little testified about?

A. That's correct.

MR. HAUG: Objection ... (Sits down and waves off objection.)

BY MS. WAYDA:

Q. Finally, Dr. Gardella, could you please turn to DDX-7.11 and take the opportunity to summarize your opinions for the Court?

A. So just to summarize in detail, I apologize for reading this, but the Raman maps show mesalamine distributed throughout the Zydus ANDA product. They provide no information on how much mesalamine is present in any one area.

And the Raman data provides no basis for Dr. Sinko to refer to it and rely on that data in support of his conclusion that the Zydus ANDA product contains mesalamine "dispersed both in a lipophilic matrix and a hydrophilic

matrix."

The optical micrographs also provide no data regarding whether or not mesalamine or excipients in the Zydus ANDA product are located in any matrix at all. They provide no information on the identity or properties of any material located in any "particles" or "granules."

MS. WAYDA: Thank you, Dr. Gardella. No further questions.

THE COURT: Thank you.

Mr. Haug, your cross-examination.

MR. HAUG: Good morning, Dr. Gardella.

THE WITNESS: Good morning.

MR. HAUG: My name is Ed Haug.

If we may approach, Your Honor?

THE COURT: You may, both the bench and the witness. Thank you.

(Binders passed forward.)

CROSS-EXAMINATION

BY MR. HAUG:

Q. Dr. Gardella.

A. Yes, Mr. Haug.

Q. Let me start by asking you a very basic question. Do you agree that it would be a basic scientific principle, that as a basic scientific principle, it is important to have as much information and data as possible before drawing

conclusions? Do you agree with that principle?
A. I agree completely, yes.
Q. Now, you know Dr. Davies quite well, don't you?
A. Yes, I do.
Q. And do you question his expertise in this area?
A. Do I question his expertise?
Q. In the area of Raman mapping, for example.
A. I think the questions I was asked to evaluate were of his data, not his expertise. So I am only questioning the details of the data and his report, and his information from his deposition.
Q. You gave a lot of opinions about what he didn't do; right? You are critiquing his data; right?
A. That is what I was asked to do, yes.
Q. Now, you have given a number of opinions. One of them is that Dr. Davies' Raman maps show mesalamine distributed throughout Zydus's ANDA product; isn't that right?
A. I don't remember the exact wording but, yes, that is a good summary of it.
Q. Do you need your slide up to read it?
A. No, no.
Q. Okay. But you agree with Dr. Davies, don't you, in his opinion and conclusion that the Raman maps show mesalamine distributed throughout the Zydus ANDA product?

Yes or no.

A. I do.

Q. You just say that there is no information about how much mesalamine is present in any one area of the product; is that right?

A. That is one of the things I said, yes.

Q. Right. But you don't dispute that there is mesalamine everywhere across the cross-section of the tablet; right?

A. Well, as I described in my deposition, I certainly found individual pixels where there was no detectable mesalamine, but that doesn't change my conclusion or Dr. Davies' conclusion.

Q. Now, you also give an opinion that the Raman data does not provide a basis for Dr. Sinko to rely on it for purposes of determining whether or not the mesalamine is dispersed both in a lipophilic matrix and in a hydrophilic matrix; is that correct?

A. That's correct.

Q. Now, you are not a pharmaceutical scientist; right?

A. I don't know how you define that.

Q. You are not an expert in pharmaceutical formulation, for example, are you?

A. Again, I want to be specific when I answer I've been very clear that I do formulation in my laboratory as a

research method, and I have published in that as a researcher; but as discussed, I think we made these distinctions very clear in my deposition. In terms of commercial products manufactured by the pharmaceutical industry, I am not.

Q. Do you even know what an "inner lipophilic matrix" is?

A. I have read the patent, and I have not been asked to opine on the definitions in the patent. And I have spent much of my career studying lipophilicity and hydrophilicity in surface chemistry, so I have my own understanding of what those words mean and what a matrix means. But I have not been asked to offer any opinions about that and have undertaken no study of the literature to draw any conclusions about that.

Q. Do you have an opinion as to whether a "matrix" is within the scope of the '720 patent?

A. No, I don't.

Q. Do you have an opinion as to what an "inner lipophilic matrix" within the scope of the '720 patent?

A. No, I have not been asked to opine --

Q. Do you have an opinion as to what --

A. -- on that.

THE COURT: Hold on.

MR. HAUG: I am sorry.

THE COURT: You have got to let him finish the answer.

MR. HAUG: I apologize, Dr. Gardella.

THE COURT: Go ahead.

BY MR. HAUG:

Q. Do you have an opinion as to --

A. I am sorry. Can I interrupt you? Can I just make sure I got on the record what I said?

Q. Sure.

A. So as I said, I was not asked to offer an opinion on that.

Q. Thank you. Do you have an opinion as to what an "outer hydrophilic matrix" is within the scope of the '720 patent?

A. I was not asked to provide an opinion about that.

Q. Do you have an opinion as to whether or not "mesalamine is dispersed both in a lipophilic matrix and in a hydrophilic matrix" within the scope of the '720 patent?

A. No, I do not.

Q. You do have an opinion, however, that I heard that Dr. Sinko was not correct to rely on the Dr. Davies' data to say that there was mesalamine dispersed both in the lipophilic matrix and in the hydrophilic matrix; is that correct?

A. That is correct. I took literally the charge that I

was given, which was to analyze the statement that I was given by counsel from Dr. Sinko's report; and I did the best, as again discussed in my deposition, to just consider the language in that statement and whether he could rely on the Raman data to make any conclusions about that.

Q. Thank you. So you do not offer any opinion on the presence of mesalamine fines anywhere that you see, do you?

A. I only understand "fines," the term "fines" as it has been discussed in this case. So, no, I have no opinion about that.

Q. You do not offer an opinion on the presence of mesalamine within the extragranular space, do you?

A. I have offered an opinion about mesalamine. I think I offered an opinion about mesalamine very clearly in a statement in my testimony here that Dr. Davies could -- data from both, as he presented in his testimony with this new information about the location of the Raman image and the granules he identified that we discussed, I did offer an opinion that mesalamine was both inside and outside the areas that he designated as a granule.

Q. And you have no opinion -- well, withdrawn.

You agree, do you not, that there are granules shown in Dr. Davies' images; right?

A. I only agree that Dr. Davies labeled something on the optical image. When asked what he meant by granules, he

labeled them and drew a G on them.

Q. In your opinion, is whatever is in that circle that he drew, there is mesalamine in there; right?

A. And outside, yes.

Q. And also outside?

A. Yes.

Q. Thank you. You have no opinion that what is shown in those images and what was circled by Dr. Davies, you have no opinion that they are not granules; right?

A. I am sorry. That is a pretty double negative complicated thing for just a silly scientist like me. So could you restate it?

Q. Certainly. Do you have an opinion as to whether or not there are any granules in those images?

A. My only opinion is to try and analyze how I understood Dr. Davies' statement that there were features, including particles and granules, that range from a particular size.

So in looking at all of the data, I could see features of many types, of many colors, of many shapes. It wasn't until the deposition that he actually labeled things that he considered particles. I was not going to draw any conclusions other than to review what he did and how he came to his conclusions. And until he circled them, I didn't know what the distinction was between a granule and another

similarly dark spot somewhere else that he didn't label.

He only labeled a few of them. That doesn't mean that he didn't consider all of the things. Just taking literally what he did, that he did not do in his report, because his report simply has a sentence, a phrase that says there are features that include particles and granules in this size range, and that was all that was in his report.

Q. Sitting here today, you have no opinion as to whether there are or aren't granules in those images; right?

A. My opinion is that he has identified granules, and my job is to try and understand what the characteristics of those granules are with respect to the data that is presented.

Q. You did not do any testing on your own; right?

A. That is correct.

Q. And you have a laboratory at your disposal where you could do Raman imaging; right?

A. I was not asked to do that.

Q. You weren't asked to do any testing whatsoever; is that correct?

A. That's correct.

Q. And did you ever advise counsel for Zydus that they should do some testing?

A. I was not asked to do that.

Q. There is no reason that you couldn't have done

testing on the samples, right?
A. I am just sticking to my statement that I was asked to do a particular thing. There was a lot of work in going through the digital data and understanding the mapping results. There wasn't a lot of information in Dr. Davies' report to do that. So that was the focus of what I was asked to do, and that is what I did.
Q. Did you talk to any of Zydus's formulators about the manufacture of the product?
A. No, I didn't.
Q. Did you review any of the Zydus manufacturing processes, for example?
A. As listed in my report, I was given that information, but all I used it for was to know the source and the type of the excipients and then use that as information that allowed me to find the reference spectra.
Q. Have you been in court the entire time of this trial?
A. Yes.
Q. So you were here for the testimony of Mr. Kulkarni; is that right?
A. Yes.
Q. Do you recall that?
A. Yes.
Q. Do you recall testimony from Mr. Kulkarni that granules are formed in the Zydus process?

A. I don't. I really wasn't playing close attention to that testimony.

Q. So do you also not recall any testimony about whether or not the magnesium stearate results in a uniform distribution within the granules produced in the compaction step?

A. I was present, but that was not part of my assignment, so I really wasn't paying close attention to those.

Q. So your opinion that you have given here today is in no way premised upon Zydus's manufacturing process; is that right?

A. That's correct. As I stated in my deposition, I have no experience with those things.

Q. Now, as I understand your criticism, if I can put it that way, of what Dr. Davies did, it is that he didn't measure the amount of mesalamine present throughout the product; is that right?

A. I just want to be clear about your entire question, if you don't mind.

So just to review, I was given his report at the time. At the time of my report, all I had was the information in his report and the digital data. And so I tried to take an objective approach to analyzing the data. I don't consider that as criticism. It is simply trying

to report the facts of the information that was provided to me.

So in the more general case of criticism, yes, that is a criticism. I don't want there to be any confusion, I didn't set out to deconstruct it or to do anything other than to analyze the data.

So I think my conclusions are that the only information that was available would not allow one to imply, take the implication that the color coding had anything to do with concentration. Nor did Dr. Davies, by the way, make any such conclusion in his deposition testimony when he was questioned.

So I don't consider that a criticism. I just consider it an analysis of what I had at that moment in time.

Q. You mentioned the colors in the Raman mapping?

A. Yes.

Q. That is the yellow, orange, red, whatever the spectrum of colors are; correct?

A. That's right.

Q. Is it correct that yellow means it is more concentrated than orange?

A. No.

Q. It is the other way around?

A. No, no. I said very clearly I was very concerned about these color maps implying something. And there was no

color scale provided in Dr. Davies' data even inside the digital files.

So I could imply and do my own analysis to show what the range of colors meant, as particularly concerned about the black areas, what did that mean. Dr. Davies said in his report that there was fluorescence that he associated with an excipient. Again, these were just words. I wanted to really make sure I understood that because images are very powerful things that are often misinterpreted, so I wanted to be clear what those meant.

And so, again, I think Dr. Davies very clearly said I am only saying it is distributed throughout. He said that multiple times. And I agree with that. And so I didn't want the implication of these maps, as they're presented, to be anything other than that.

Q. Thank you. You just don't know how much mesalamine is located across the cross-section of the tablet; right?

A. No one knows.

MR. HAUG: Can we have PTX-1 up, please.

BY MR. HAUG:

Q. You said you reviewed the patent; right?

A. Yes.

Q. Did you read it?

A. I read it.

Q. We'll have it in a second. I am going to ask you to

look at claim 1.

Did you read claim 1?

A. Yes, I did.

MS. WAYDA: Objection, beyond the scope of direct.

THE COURT: I don't know whether it is or not. Let's hear the question.

BY MR. HAUG:

Q. Is there anything in claim 1 that speaks to how much mesalamine needs to be anywhere?

A. I am not offering an opinion at all about the details of claim 1. I just simply read it, and, again, if I could tell you that I used it to understand what excipients were at issue here. And then I further refined that by looking at the Zydus ANDA information to get exactly which excipients would be needed to collect reference spectra.

Q. Are you aware of the claim construction in this case?

A. No, I am not. I have, I have been given certain definitions but the overall claim construction I have not read.

Q. Those are definitions that were given to you by Zydus's counsel; is that correct?

A. That's correct.

Q. But you don't really understand them beyond what was given to you, is that right?

A. Sir, I wasn't asked to offer any information related to the claims.

Q. So, for example, you didn't read the Court's claim construction about the word "dispersed" as used --

A. I remember having a discussion about that but since the word dispersed wasn't used in Dr. Davies report, I followed what, you know, the language that he used and not -- all I understand is there is a very specific definition for dispersed.

I think I have heard it but it wasn't a factor in anything that I considered.

Q. Well, can I have DDX-7.11 up, please?

This is one of the slides of your book.

There we go. 7.11. Thank you.

Second bullet. Your opinions, summary of your opinions, Dr. Gardella. At the end, you say, the Zydus ANDA product contains mesalamine "dispersed both in a lipophilic matrix and in a hydrophilic matrix."

Did you write that or was that Zydus counsel?

A. Zydus counsel gave me that phrase and quotes from Dr. Sinko's report, as I understood it.

Q. So is it fair to say that Zydus's counsel created this slide for you?

A. No.

Q. You wrote it?

A. I wrote it.
Q. So?
A. It's pretty close to exactly what was in my report.
Q. Sitting here now, do you have an understanding of what is meant by the quoted language?
A. I, sitting here now? Yes, I do.
Q. What is it? What does "dispersed both in a lipophilic matrix and in a hydrophilic matrix" mean to you?
A. It just means that the mesalamine is present throughout both of those structures.
Q. Let's talk a little bit about excipients. You have also critiqued what Dr. Davies did in the sense that he didn't locate, if I can put it that way, the location, or he didn't find the location of excipients. Is that right?
A. I don't think that is a critique. I think I analyzed his data because, again, in his report, he didn't say anything. He mentioned excipients, especially with respect to fluorescence. He didn't indicate that in his report, he didn't indicate that he considered what the reference spectra of the excipients were and so I only had the information in his report and I undertook what I would normally do if I was in his shoes. And that is to collect the information on the excipients and make sure that it didn't, it wasn't present. I just, everything that I said in my testimony earlier --

Q. Are you saying --
A. -- they set a reference to.
Q. Are you finished?
A. (Nodding head.)
Q. I am sorry. Thank you.
Are you saying there are no excipients in the Zydus ANDA product?
A. No, I am not saying that at all.
Q. Did you hear the testimony that Mr. Kulkarni gave about excipients.
A. Again, I wasn't paying close attention to that testimony. I was just present.
Q. In any event, you didn't do an analysis yourself about whether or not excipients are in the Zydus product and where they might be located?
A. I think I did an analysis to see if Dr. Davies' Raman data showed any evidence of those things, and I described what, I think very clearly what the steps would have been had I been able to see signals that detected them in Dr. Davies'. Following depositions, I got more, you know, there were more details of what he considered. But at the time, I started with no preconceived notions about it. I knew what the excipients were. I certainly believed they're in the formulation. And it was my task to examine the data.
MR. HAUG: Could we have DDX-711 again, please?

BY MR. HAUG:

Q. I'd like you to focus on the third bullet point: Optical micrographs provide no data regarding whether or not the mesalamine or excipients in the Zydus ANDA product are located in any matrix at all.

Is it still your testimony that the optical micrographs provide no data regarding whether mesalamine is in the product?

A. That's correct.

Q. It is or isn't your testimony that you agree it is in the product?

A. I agree it is in the product.

Q. Well, this says optical micrographs provide no data regarding whether mesalamine is in or excipients are in the Zydus product and located in any matrix at all; right?

A. Optical micrographs simply are the response from lighting, shining a light on the sample and taking a photograph of it. They contain no chemical information, no chemical information to identify what is there. And I don't -- sorry -- I don't believe Dr. Davies did anything other than report them.

As I learned during his depositions, this is a standard technique that they do when they cut a cross section is to take a series of optical micrographs and as he said multiple times during his deposition, he provided all

that digital data so we could examine them but, fundamentally, as he also testified, they don't say anything about the composition, meaning the identification of what is mesalamine and what are excipients.

Q. So if you combine the data provided in the optical micrographs with the data from the Raman data, could you then determine whether or not the mesalamine is in the Zydus product?

A. I think the Raman data provide Dr. Davies the information that show the mesalamine is distributed. That's the only experiment that was done that contained chemical information that I examined and had, as Dr. Davies said, a spectrum that could be used to identify mesalamine and only mesalamine.

Q. Can you go to Tab 13 in your book, please?

A. Sure.

Q. And I'd like you to look at PDX-2.9.

A. 2.9, yes.

Q. Okay. You recognize this as coming from Dr. Davies' testimony and testing; right?

A. Yes, I do.

Q. Given your view that mesalamine is throughout the product, wouldn't you agree with me that there is mesalamine both inside and outside the volumes marked at granules by Dr. Davies?

A. I think I said that in my direct testimony, yes. I should say that this was the first time in his testimony that any of this sort of spacial location was provided. So it comes as somewhat of a surprise.

Q. In any event, you agree with it?

A. I do.

Q. Now, at the beginning of your testimony, you said that you have testified a number of times in other cases. Do you recall that?

A. Yes.

Q. Okay. And --

A. I listed the last times in my report.

Q. Okay. And you also, at the beginning of this cross, I asked you whether or not you agree with the basic scientific principle that it is important to have as much information and data as possible before drawing any conclusions, and that you agree with that; isn't that right?

A. I think generally, yes.

Q. Have you ever been found by any court to have contradicted that basic principle?

A. You will have to explain what you mean by that.

Q. If you go to tab 11, please, in your binder.

A. (Witness complies.)

Q. Do you have it?

A. Tab 11, yes.

Q. Tab 11. It is a case there that says Elan Corporation v Andrx Pharmaceuticals. Do you see that?
A. Yes, I do.
Q. Do you remember being involved in that case?
A. Yes, I do; with Judge Jordan but a different Judge Jordan in Florida.
Q. And you testified in that case, didn't you?
A. Yes, I did.
Q. If we go to page 44 of this opinion. It is actually, yes, page 44 in the lower right.

Do you see up at the top of the right-hand column?
A. Yes.
Q. It says: Dr. Gardella's Interpretation of the TOF-SIMS Test Results, and it goes on. Do you see that?
A. Yes.
Q. And from there, which starts with paragraph 544, in the Court's findings of fact and conclusions of law, it goes all the way through to paragraph 604, talking about your testimony that you gave in that case, doesn't it?
A. Yes. It's been a long time since I have seen this. Yes.
Q. Well, this decision, when was this decision? It was in 2008; right?
A. I don't remember when the decision in the Elan case

came. The testimony was long before that.

Q. The date I was referring to appears on the first page of the decision. Anyway, I'd like you to look at paragraph 553.

And the Court found: Dr. Gardella formed his expert opinion without reviewing Andrx's ANDA, except for the summary flowchart it contains [trial transcript at 1621 (Gardella)]. Dr. Gardella agreed that the ANDA contains a vast amount of detailed technical information relating to the manufacture and composition of the Andrx product.

If we can go on to the next paragraph, 554.

When he wrote his report, Dr. Gardella was unfamiliar with the dissolution profile of Andrx' product. Dr. Gardella could not describe the dissolution equipment type 1 and type 2 according to the U.S. Pharmacopeia.

Did I read all that correctly?

A. I was not asked to do any of that work. I was asked -- again, I had a very limited charge in that case. So all of those are facts, but I think they're limited by what I was asked to do in that particular case.

Q. So is it the case that in the Andrx case, you were also confined to just the very narrow investigation, similar to this case? Is that what you are saying?

A. Yes, that is what I recall. It's been a long time.

Q. I'd like you to go to paragraph 594.

And the Court's findings of fact and conclusions of law, it is stated, 594: Dr. Gardella agreed that, as a scientist, it is important to have as much information and data as possible before drawing conclusions, and he "firmly believe[d]" in this basic scientific principle. [Trial transcript at 1614 (Gardella)]. Yet Dr. Gardella contradicted himself by testifying that it would not have been important for him to know what his own test results were before drawing any conclusions about Elan's test results.

Did I read that correctly?

A. Yes, you did.

MR. HAUG: Thank you, Dr. Gardella. No further questions.

THE COURT: Any redirect?

MS. WAYDA: No, Your Honor. We conclude our examination of Dr. Gardella.

THE COURT: Okay. Thanks, Dr. Gardella. You may step down.

THE WITNESS: Thank you.

THE COURT: Your next witness, please.

MR. GAERTNER: Your Honor, Mike Gaertner. We're going to be playing a few short deposition transcripts in. We'll give them to you in just one moment.

THE COURT: Okay.

MR. BLEIBEL: May I approach?

THE COURT: You may.

MR. BLEIBEL: Thank you.

(Binders passed forward.)

MR. BLEIBEL: Good morning, Your Honor.

THE COURT: Good morning.

MR. BLEIBEL: Wasim Bleibel for Zydus.

The first video we will play is that of named inventor on the '720 patent, Roberto Villa. Mr. Villa's deposition was taken over two days, so these two video clips will be played in sequence.

At the time the deposition was taken, he was the plant director at Cosmo, and he was identified as of the 30(b)(6) witness on the formulation and manufacturing process for 1.2 gram delayed release mesalamine tablets.

And I will just warn you that in the second part of this, of his deposition, it gets to be a little confusing to follow what is going on, and so I'll just explain to you he is asked by Mr. Parr to identify in his lab notebooks examples that are shown in the '720 patent. Those examples are illustrative of the invention, as they termed it, in greater detail.

So at the conclusion of the deposition portion, if the Court would like me to walk them through the batch numbers, the notebooks, and the page numbers, I would be

more than happy to.

THE COURT: Let's watch the video.

(Video played of Roberto Villa.)

"Question: Could you, for the record, state your full name?

"Answer: Roberto Villa.

"Question: And what is your current position at Cosmo S.p.A.?

"Answer: Plant director.

"Question: In connection with the development work to develop a controlled release formulation of mesalamine, did you or the formulators working at Cosmo attempt to develop a controlled-release formulation of mesalamine using a single matrix?

"Answer: Absolutely no. Because, as far as I can remember, it could be easily proved that you could not have extended release having a single matrix.

"Question: And what did you base your recollection or your remembering on?

"Answer: My recollection is based on the fact that we have experience with an active in -- 1,200 milligrams of active ingredient in a tablet that does not weigh more than 1 gram. 1.5 grams.

"Question: Did you have any prior experience, before doing the formulation work to develop a controlled-

release formulation of mesalamine, with any drug product where the amount of active ingredient in the tablet was only 1,200 milligrams but the tablet itself did not weigh more than 1.5 grams?

"Answer: No. It's only my knowledge and the common sense that you cannot produce a formulation of that kind.

"Question: And just to make the record clear, did you attempt to do any test to determine whether mesalamine could be formulated in a controlled-release formulation using a single matrix?

"Answer: Yes. A number of preliminary trials were performed.

"Question: I'd like to direct your attention now to the claims of this '720 patent, which start on column 6 at line 7.

"The Witness: Si.

"Question: Do you see claim 1 has three sub-parts -- subparagraphs to it, Mr. Villa?

"Answer: Yes. a), b), and c).

"Question: And c) states, quote: 'Optionally other excipients.'

"Do you see that?

"Answer: Yes. Exactly.

"Question: And looking at claim 1, which is a

composition claim, where do these other optional excipients belong or fit in the composition?

"Answer: It's the same question that you asked me earlier on -- earlier on. These agents are all excipients that are included in all outer formulations, which are the disintegrating agents, flow agents, lubricants, and so on.

"Question: Did you contemplate that any of these other excipients could be included in the inner lipophilic matrix?

"Answer: I would say absolutely no as lipophilic substances.

"Question: Do you mean that the items that you mentioned, 'disintegrating agents, flow agents, lubricants, and so on' are not lipophilic substances?

"Answer: As far as I know, the only substance which could be considered as lipophilic but is not used as a lipophilic agent could be the magnesium stearate.

"Question: The question was: 'And what do you base that statement on?'

"And the statement that the witness made, as, as it appears on my screen, and I am basing it on an interpretation, obviously, and then the reporter's reporting of it, it says: 'As far as I'd know, the only substance can -- could be considered as lipophilic but is not used as

a lipophilic agent could be the magnesium stearate?'

"Answer: I base this on -- I base this statement on our formulation, especially, because we used an amount of magnesium stearate which is 14 milligrams, 1 percent only of the formulation, only in the outer phase.

"And we add this only by mixing the final product for ten minutes.

"And, therefore, in this statement it is considered, by all the holy texts, it is considered as a lubricant. 'Lubricant' means that it allows for the tablet to be removed from the device that makes it only after it has been formed. And it has no in inference at all on the dissolution of the final product.

"This is my experience. And it is the product of all my work of trial and formulation of Alda (phonetic).

"Mr. Haug: Lialda.

"The Interpreter: Lialda. I am sorry.

"Question: Mr. Villa, when you talk about the use of magnesium stearate, are you referring to the commercial product that is manufactured by Cosmo and sold as Lialda?

"Answer: I am referring to the commercial product line, which is sold. But I am also referring to all the other products that I have studied and participated in the formulation of which use the magnesium stearate only as

a lubricant.

"Question: When you mentioned that you used magnesium stearate which is 14 milligrams, 1 percent only of the formulation, what do you mean when you mentioned the words '1 percent only?'

"Answer: Because in all the holy texts of pharmacology and formulations, when we speak of magnesium stearate used as a disintegrating agent, we can employ only 1 percent, no more than that.

"Question: And when you refer to the 'holy texts of pharmacology and formulations,' what specific texts are you referring to?

"Answer: I am referring to the Pharmacopeia and to the handbooks that are available in all development laboratories and in all pharmaceutical industries.

"Question: Earlier, when you mentioned 'the holy texts,' you referred to speaking of magnesium stearate used as a disintegrating agent.

"What is a disintegrating agent?

"The Witness: Sorry. I just make a mistake, but magnesium stearate is a lubricant.

"Question: And if there is not enough magnesium stearate is a tablet, will the embossing, identification print be affected by the lack of sufficient magnesium stearate?

"Answer: It's not only the print on top of the, on the tablet, but it's, it's the whole process that is affected. For example, if you have a sticking defect, that means that the whole -- and, and it means that the tablet actually sticks to the machine that makes it. And, therefore, the whole, the whole tablet is jeopardized. The use of this product is related merely to the mechanical action.

For the formulation of Lialda, this is what happens. I don't know about the rest.

(Video ends.)

MR. BLEIBEL: This is the second portion.

THE COURT: All right.

(Video played.)

"Question: I'd like to have the court reporter hand to you now what has been previously marked as DDX-104.

"I am showing you what has been marked as DDX-104 previously.

"Mr. Villa, is this a document -- can you identify this document for the record first?

"Answer: This is a laboratory notebook, which is a record of all the analyses that are performed during pharmaceutical development.

"Question: I'd like you to turn now to a document that is marked previously as DDX-105.

"The Witness: Si.

"Question: Mr. Villa, during the break, were you able to go and find the source information for the examples that are set forth in the '720 patent?

"Answer: Yes.

"Question: And what were you able to locate?

"Answer: I was able to locate the lot numbers that refer to these examples. And they are to be found in notebooks 2 and 3.

"Question: Okay. And do you have documents that show which lot numbers there are -- they are?

"Answer: Yes. I can tell you that Example 1 refers to Lot Nos. 5209 and 5210, in Notebook 2.

"Question: Can you hand up, Mr. Villa, the document marked as DDX-106? That's an official lab notebook.

"The Witness: Si.

"Question: And is that on page COMESA7373 of Deposition Exhibit No. 104?

"Answer: Exactly.

"And then it continues on Notebook 3.

"Question: Example 1. Okay.

"Example 2?

"Answer: Example 2 is 5218-2.

"Question: Let's go back just briefly to

Example 1. And you mentioned that it continues on to Notebook 3.

"Can you, first of all, tell us where in Notebook 3 it continues on to?

"Answer: 5209 and 5210.

"Question: Do you know the page numbers, COMESA numbers?

"Answer: 7378. 7373.

"Question: Can you read the, the first page, the COMESA number for the first page of the experiment, and continue to the end of the experiment, the COMESA number?

"Answer: 7373 'til page 7378.

"Question: Okay. Thank you.

"Lot 5210, where is that one, then, in the --

"Answer: In one of the pages that I just mentioned.

"Question: Let's move on to Example 2 of the '720 patent. And if you can identify the pages, and it's best if you do it by the COMESA number, the beginning and the end.

"Answer: COMESA, Example 2 is COMESA 7379, 7380.

"Question: Do you have the lot number for that example? The lot number.

"Answer: 5218/1.

"Question: And for Example 3, then? What is the lot number for Example 3?

"Answer: 5223/1.

"Question: And can you find it in the lab notebooks then? Or, actually, Mr. Villa, if you just give us the lot numbers for each of the other examples --

"The Witness: Yes, yes.

"Question: -- I think that will be satisfactory. We can, we can find it ourselves.

"Answer: The lot number for Example 3 is 5223/1.

"Example 4 is 5218/2.

"And Example 5 is 5223/2.

"Question: I would like to direct your attention now to the third lab notebook, which is DDX-106.

"Answer: Yes.

"Question: And let me ask you to look at the Bates page stamped COMESA7177.

"Actually, this, I think it's the Lab Notebook No. 1.

"Answer: No. 1. Okay.

"Question: Yes. Whose signature is there on this particular lab notebook?

"The Witness:: Mine. It's only the initial.

"Answer: This is my signature, not in full.

It's only the initials.

"Question: In the sentence that appears in this lab notebook on page 7188, the page that you initialled as 'read and understood,' the sentence that appears at the top is a, is a full sentence, is it not? 'Reduction in the quantity of magnesium stearate and introduction of lipophilic excipients.' Correct?

"Answer: Yes. The object of this lab test is exactly as described.

(Video ends.)

THE COURT: All right. The thing that would be helpful to have on the record is how the -- and it doesn't have to be done right now but the correlation between the DDX numbers and the trial exhibit numbers they referred to.

Mr. Parr, in the deposition, was questioning him and the witness was responding with respect to documents identified by DDX numbers, which I assume are deposition exhibit numbers. If those things are in the record now under a different number, and it appears they were from the questions on the scene because there were separate stick numbers that were trial numbers, you should put into the record some kind of a document indexing those two numbers so that I can know what is being talked about. And I'll leave it to you and opposing counsel to agree on that and get it into the record. All right?

MR. BLEIBEL: Thank you, Your Honor. We will do that.

THE COURT: All right. What else do you have for me?

MR. BLEIBEL: At this time I would move into evidence DTX-28, DTX-29, DTX-57, DTX-58, DTX-59, and DTX-60.

MR. HAUG: No objection.

THE COURT: Okay. Fine. They're admitted without objection.

(Above-referenced exhibits are admitted into evidence.)

THE COURT: Do you have the DDX numbers that those correspond to?

MR. BLEIBEL: I do.

THE COURT: Go ahead, read those in and we'll take care of it right now.

MR. BLEIBEL: So DDX-104 is DTX-57 and 58.

DDX-106 is DTX-28 and 29.

And DDX-105 is DTX-59 and 60.

THE COURT: Okay. Thank you.

Do you have anything else?

MR. BLEIBEL: We have one more video clip.

May I approach?

THE COURT: Sure, you may.

(Binders passed forward.)

MR. BLEIBEL: Just to make the record clear, the notebooks I moved into evidence just a moment ago, let me state --

THE COURT: The exhibits?

MR. BLEIBEL: Correct. The exhibits I moved into evidence, 57, 28, and 59 were the Italian notebooks.

MR. HAUG: Objection. Objection. Your Honor, I am sorry to interrupt, but I object to attorney argument which I think is what this is going to be, correlating documents. If it's in the record and it can be correlated, we can do that post-trial.

THE COURT: Yes. I don't want you testifying, Mr. Bleibel. If you have got a way to correlate the information, that is fine, but don't start telling me what things are unless you have got agreed on bases for telling me what things are, okay?

MR. BLEIBEL: Very good.

THE COURT: All right. Good enough.

MR. BLEIBEL: All right. The next deposition designation we'll be playing today is Loyd Allen. At the time Mr. Allen's deposition was taken, he was Shire's originally offered expert on melting point.

THE COURT: Okay.

(Video was played as follows.)

"Question: Could you please state your full

name for the record?

"Answer: Okay. It is Loyd Vernon Allen, Jr.

"Question: You're the author of the mag stearate monograph in the Second Edition of the Handbook of Pharmaceutical Excipients, correct?

"Answer: Correct.

"Question: Looking at sentence, though, Steffens indicates that the melting point provided in the handbook is incorrect; correct?

"Answer: No, that's not what this is saying; because you can see other articles where it definitely states at the beginning a melting is 88, 89 degrees, and it has been interpreted that way for many years.

"Question: So in putting together the handbook monograph for the Second Edition, you just ignored this physical property information in Steffens; correct?

"Answer: I didn't ignore that information, but during the Second Edition, I pretty well took the specifications in the front end and spent more time on the comments in the parts of the second half of the monograph.

"Question: So are you saying you just pretty much took specifications of the First Edition and didn't futz with them; is that correct?

"Answer: I just reviewed them real quickly in Merck Index, chemical handbooks, and if they were correct

there, then I kept them in.

"Question: So you didn't actually look at the scientific literature to see whether there had been a change in how people in the industry thought about melting point at that time; correct?

"Answer: No, not in the specifications.

"Question: Dr. Allen, if you look at paragraph 30 of Exhibit Allen 1, in your report. When it came time to do the Third Edition of the Handbook of Pharmaceutical Excipients, you say the editors requested that all monographs be updated; is that correct?

"Answer: Yes.

"Question: And was there a reason for updating all the monographs?

"Answer: It was just periodically whenever you're doing a large volume like that, the editors or individual authors may go in and do additional work. Like right now with Remington's, I have asked all my authors to really go through and do an in depth revision of each of those chapters.

"So it doesn't happen in every edition. You just sometimes simply update and then sometimes you do a lot of revision and updating.

"Question: You attached that Third Edition to your report as Exhibit 6; correct?

"Answer: I believe that's correct.

"Mr. Abramowitz: I will mark as Allen Exhibit 7, the Handbook of Pharmaceutical Excipients, Third Edition, that was attached as Exhibit 6 to his report.

"Question: I just ask that you confirm for me that this is the Exhibit 6 attached to your report.

"Answer: Okay.

"Question: You state in paragraph 30, 'Additional effort was expended and suppliers of the excipients were contacted to provide their specifications resulting in some changes in the monographs;' is that correct?"

"Answer: Correct.

"Question: And did you, for the purpose of the magnesium stearate monograph, did you contact additional suppliers to get additional information?

"Answer: Yes.

"Question: One of the properties that you changed in the third edition of the magnesium stearate monograph was the melting range; is that correct?

"Answer: Correct.

"Question: The melting range was revised to 117 to 150 degrees C for commercial samples and 126 to 130 C for high purity magnesium stearate; is that correct?

"Answer: Correct.

"Question: Would you say that this information that you revised in the third edition of the handbook represents an update of how the industry viewed the melting point of magnesium stearate?

"Answer: It appeared to me that the industry was going more towards the specifications for the anhydrous form of magnesium stearate, which is reflected -- which is one of the four forms of magnesium stearate that we talked about, and they were listing these ranges in their current certificates of analysis.

"Question: But if the hydrated form melted at a lower temperature than 105 degrees C, would this process not have worked?

"Answer: As it is being heated, there can be some changes in the crystalline structure where, as the water is given off, part of the matrix may liquify, and then as the water continues to be given off, the crystalline structure changes to a higher melting point magnesium stearate, which is common with polymorphic materials like this.

"Question: So to actually determine the melting point of the sample that was used in Zydus's product, someone had to test it; correct?

"Answer: Correct.

"Question: Is there an appropriate method to

use to test that sample in order to determine its melting point?

"Answer: Obviously, the most common is DSC.

"Question: You state at 47, 'The removal of water may be accompanied by a change in crystal structure or changes in the solid state.' Do you see that?

"Answer: Yes.

"Question: You said, 'This change in structure can be called a solid-solid phase transition;' is that correct?"

"Answer: Yes.

"Question: So this endotherm at 90 in Allen 33, or approximately 90, could be called a solid phase transition; correct?

"Answer: Could be, yes.

"Question: And that would not be considered a melting; correct?

"Answer: Well, it could also be called a solid -- or a liquid-solid or a solid-liquid phase transition for a small component, which would be a mesomorph, but I don't have any data for that.

"Question: You have no data that supports that it was a solid-liquid-solid transition or anything else; correct?

"Answer: Correct.

(Video ends.)

MR. BLEIBEL: And that's the conclusion of the deposition designations for Loyd Allen.

THE COURT: All right. Thank you. Your next witness.

MR. PETERKA: Good morning, Your Honor. Defendants call Dr. Umesh Banakar.

MR. MILLER: May I approach, Your Honor.

THE COURT: You may approach the bench and the witness.

(Documents passed forward.)

... UMESH BANAKAR, having been first duly sworn, was examined and testified as follows ...

THE COURT: Hi. Good morning. Please have a seat.

Mr. Peterka, you may proceed.

MR. PETERKA: Good morning, Dr. Banakar.

I am told we're waiting on our slides. Hang on one second, Your Honor.

DIRECT EXAMINATION

BY MR. PETERKA:

Q. While we're waiting, can you state your name and current address for the record?

A. Yes. First name, Umesh, U-m-e-s-h. Last name Banakar, B as in boy, a-n-a-k-a-r.

Q. And your address?
A. My address is 10251 Tammer drive, T-a-m-m-e-r, Drive, Carmel, Indiana 46032.
Q. Have you prepared a slide presentation to help us today in our discussion?
A. Yes, I have.
Q. Thank you. If we could turn to slide 2. I'd like to talk a little bit about your qualifications to start with.
Are you currently employed?
A. I am self-employed. I provide technical consults and consultation to pharmaceutical industry and activities worldwide in the areas of pharmaceutical formulation development, the evaluation particularly in dissolution testing and also in human subjects.
THE COURT: Doctor, would you mind just pulling that microphone a little closer to you?
THE WITNESS: Sure.
THE COURT: Thank you.
BY MR. PETERKA:
Q. Do you also teach formulation development and evaluation to the pharmaceutical industry?
A. Yes. I teach these courses or I teach development of pharmaceutical formulations to various groups which cover pharmaceutical industry as well as associations, colleges, so on and so forth.

Q. Can you please describe your education?

A. I have a Bachelor's Degree in Pharmaceutical Sciences, and I have a Doctorate in Pharmaceutical Technology with minor in Pharmaceutical Chemistry.

And I have also training which is through a very focused program on controlled release technology.

Q. Before you were a consultant, where did you work?

A. I was a professor at three places.

One is, the first one I started off with was at Creighton University in Omaha, Nebraska.

Then I was recruited at St. Louis College of Pharmacy as Director of Research and Chairman of Pharmaceutical Sciences division.

And then last one was at Butler University School of Pharmacy where I was Chairman of Graduate School as far as Chairman of Pharmaceutical Sciences division.

MR. PETERKA: Can I have the next slide, 3, now.

BY MR. PETERKA:

Q. Can you talk about some of your recognition and awards?

A. Over the course of my career, I have received numerous awards in teaching and scholarly activity, and also contributions to pharmaceutical sciences worldwide. Some of the noteworthy ones are on the slide.

I have done four assignments for the United

Nations in which two were awarded Service to Country Award by United Nations.

More recently, I was conferred the Outstanding Contributions to Dissolution Science Award by the Society of Pharmaceutical Dissolution Science.

Q. Thank you. Are you a member of any professional organizations?

A. Yes. I am a member of numerous professional organizations over the years. One of the noteworthy ones that I want to mention here is I founded the Society For Pharmaceutical Dissolution Science, the first one of its kind in the world. And I am also the Chairman of the Scientific Affairs aspect of it.

MR. PETERKA: Next slide, please.

BY MR. PETERKA:

Q. Can you just talk a little bit about your publications?

A. I have various publications in various formats in area. I have over 100 research articles, numerous chapters in various textbooks.

I have several focused technical manuals.

I have textbooks written on dissolution, pharmaceutical dissolution testing, pharmacokinetics, and the most recent one has been the Desk Book of Pharmaceutical Dissolution Science and Applications.

And recently, a six volume, 93 chapter series was published on NanoBioMedicine.

Q. Are you also a reviewer for any scientific journals?

A. Yes. I am a reviewer for numerous scientific journals and also been on the member of various editorial boards, have had 92 publications authored over the years.

Q. Dr. Banakar, have you previously testified as an expert in pharmaceutical cases?

A. Yes, I have.

Q. Have you ever testified on behalf of Shire?

A. Yes, I have.

Q. Have you been accepted as an expert in the areas of pharmaceutical formulation and evaluation, including controlled release technology and dissolution testing in those cases?

A. Yes, I have.

Q. Is there anything else that you think further demonstrates your expertise in the field of pharmaceutical formulation evaluation?

A. Yes. I would like to mention that I have developed, personally developed hundreds of pharmaceutical formulations over the time span of 20-30 years that I have been in the course of my career.

These formulations have been of various types: Solid dosage forms, liquids, et cetera. Immediate release

formulations, controlled release formulations.

Over 100 of those formulations have been for U.S. market.

In addition to that, I have done thousands of dissolution testings in my career, and I continue to do that even today.

Q. Can you turn in your book to DTX-3, please.

A. I don't have a book here.

Q. Oh, you don't.

MR. PETERKA: May I approach?

THE COURT: You may approach.

(Binders passed forward.)

BY MR. PETERKA:

Q. All right. Let's try that again. Can you turn to DTX-3 in your book?

A. Yes.

Q. Is this a copy of your CV?

A. Yes, it is a copy of my CV.

Q. And the information in the slides and additional information we were just talking about, is that all reflected in the CV?

A. Yes, it is as current as October 2014. There would be additions which would not be in there.

MR. PETERKA: I ask the Court recognize Dr. Banakar as an expert in the areas of pharmaceutical

formulation and evaluation, including controlled release technology and dissolution testing.

MR. HAUG: No objection.

THE COURT: All right. We'll hear him as an expert.

MR. PETERKA: Thank you.

I believe your next slide, can I go back to the presentation? Slide 5.

BY MR. PETERKA:

Q. This is a copy of the '720 patent?

A. Yes.

Q. Have you reviewed the '720 patent as has been discussed during this trial?

A. Yes, I have.

Q. Have you reviewed the prosecution history?

A. Yes, I have reviewed the prosecution history for the '720, the '720 patent itself, various reports that have been submitted over the period of this case.

I also looked at data and experimental work that was provided in this matter.

And I have also applied my personal experience in development.

Q. I take it as a general basis, those are the bases for the opinions you can express?

A. That is correct.

Q. Are you familiar with the Court's claim constructions in this case?

A. Yes, I am.

MR. PETERKA: The next slide. This is slide DDX-10.6.

BY MR. PETERKA:

Q. Are these the Court's claim constructions that you are familiar with?

A. These are the terms and the constructions provided by the Court. They are the claim constructions which I have just stated in numerical order -- sorry, alphabetical order.

Q. Did you apply those constructions in forming your opinions in this case?

A. Yes.

MR. PETERKA: Can I go to the next slide, please?

BY MR. PETERKA:

Q. Dr. Banakar, in general, what will you be testifying about today?

A. Today, I am testifying whether Zydus's ANDA product infringes claim 1 or claim 3 literally and under the Doctrine of Equivalents.

Q. Have you formed an opinion as to whether Zydus's ANDA product will infringe claims 1 and 3 of the '720 patent?

A. Yes, I have formed an opinion. That opinion is

Zydus's ANDA product does not infringe claim 1 and claim 3 of the '720 patent both under literal as well as under Doctrine of Equivalents.

Q. And why, in your opinion, does Zydus's proposed ANDA product not infringe the '720 patent claims, claims 1 and 3, sir?

A. The overview for noninfringement is based on this slide where the claimed matrix, Zydus does not have the inner lipophilic matrix, does not have the outer hydrophilic matrix, and the active ingredient mesalamine is not dispersed both in the lipophilic and in the hydrophilic matrix.

Q. Do those opinions apply to both claims 1 and claim 3?

A. That is correct.

MR. PETERKA: Go to the next slide, please.

BY MR. PETERKA:

Q. Breaking down your noninfringement opinions further. Why does Zydus's ANDA product, in your opinion, not have the claimed "inner lipophilic matrix?"

A. There are several reasons why that is true. The alleged "inner lipophilic matrix" does not consist of the required excipients.

Additionally, it does not have the required structure.

Furthermore, it does not exhibit lipophilic

properties.

And it does not function to control the release of the drug.

Q. Thank you.

MR. PETERKA: Next slide, please.

BY MR. PETERKA:

Q. I'd like to go to your first point that was on the earlier slide there. The first reason Zydus's ANDA product does not have the claimed "inner lipophilic matrix," I believe that was the magnesium stearate used in the Zydus ANDA product does not have a melting point below 90 degrees C; is that correct?

A. That is correct.

Q. Based on your experience in pharmaceutical formulation, how would one determine the melting point of a particular substance?

A. The melting point of a particular substance is determined by the standard test which is provided in United States Pharmacopeia or USP which has the controlled or standard required to perform the test which is in the monograph in that USP.

MR. PETERKA: Can I have the next slide, please.

BY MR. PETERKA:

Q. And what is on this slide?

A. This slide is the excerpt of melting point range or

temperature determined or procedure that is to be determined to be followed and the standards and controls to be followed as in monograph 741 in USP.

Q. And are these from, this is from DTX -- I think there is two versions on here; right?

A. That is correct.

Q. Can you explain those different versions?

A. DTX-72 is 1995 USP. DTX-52 is the second supplement, 2014 USP 37 National Formula 32.

THE COURT: Mr. Peterka, if you are going to ask him, I won't, but what is the difference between the two?

THE WITNESS: 2014 is the updated current one.

THE COURT: That much I am with you on, but is there a substantive difference between those two?

THE WITNESS: The standards and controls are the same.

THE COURT: So there is no substantive difference between those two?

THE WITNESS: The editions have different temperatures.

THE COURT: Okay. I'll let you question.

BY MR. PETERKA:

Q. This is the monograph that you and Dr. O'Halloran talked about earlier; correct?

A. That is correct.

Q. Have plaintiffs' experts conducted the USP melting range or temperature test on the magnesium stearate used in the Zydus ANDA product?

A. No, the plaintiffs have not done the USP. They are not following the USP melting range and melting temperature procedure for formulating the melting point of magnesium stearate.

THE COURT: And I should make clear what I'd said between "these two." I was a little unclear on the record. I apologize.

I was looking at DDX-10.10 and the excerpted language you had put up there from the two versions of the USP, the 1995 version around the 2014 version. That was the basis of my questions to Dr. Banakar. Just so it is clear on the record.

MR. PETERKA: All right. Thank you, Your Honor.

THE COURT: Please continue, Mr. Peterka.

BY MR. PETERKA:

Q. Did you hear Dr. O'Halloran's testimony this morning?

A. Yes, I did hear Dr. O'Halloran's testimony this morning.

Q. And you reviewed his test results?

A. Yes, I have reviewed his test results. They are on the next slide.

Q. Did Dr. O'Halloran follow the USP procedure?

A. That is correct. He did.

MR. PETERKA: Can we have the next slide.

BY MR. PETERKA:

Q. And what is on this slide, Dr. Banakar?

A. This is the slide where Dr. O'Halloran's test results are in that table where it shows that the temperature at which magnesium stearate sample began to melt was, is at 143 degrees Celsius, and it completely melted, end of melt, at 145.5 degrees Celsius, within that range.

Also, the sample, the sample number indicates the sample where it came from. It came from the same lot of magnesium stearate that was used in Zydus ANDA batch EMM196. And the producer of that excipient magnesium stearate is Dr. Lohmann.

MR. PETERKA: Can we go to the next slide.

BY MR. PETERKA:

Q. And this is what you were just talking about?

A. That is correct.

Q. Now, what does this show?

A. This shows the material I just covered. The top box.

MR. PETERKA: Just for the record this is DDX-10.13.

BY MR. PETERKA:

Q. Sorry. Go ahead.

A. The top box is where the magnesium stearate is from,

Dr. Paul Lohmann.

This is the number, sample number. That is the batch number that came from.

Q. And that corresponds to the batch you referred to earlier?

A. That is correct. If you go to the previous slide, that is the sample number.

Q. Okay. And the top document in this slide, that is an excerpt in the Zydus batch manufacturing record; is that correct?

A. That is correct.

Q. And that is DTX-18?

A. That is correct.

Q. Can you turn in your binder to DTX-18, please?

A. (Witness complies.) Okay.

Q. And that is the batch manufacturing record for the Zydus ANDA product, EMM196?

A. That is correct.

Q. Can we go back to the slide we were just on? And the bottom document that you were just matching up, the batch number, the Zydus batch number with the vendor batch number, that is from DTX-48. Can we turn to DTX-48 in your book?

A. Yes.

Q. And what is DTX-48?

A. DTX-48 is the Quality Control Department Certificate

of Analysis for magnesium stearate.

Q. This is for the magnesium stearate in the EMM196 product?

A. That is correct.

MR. PETERKA: Okay. To the extent it is not in already, I'd move DTX-48 into evidence.

MR. HAUG: No objection.

THE COURT: It's admitted without objection.

(DTX-48 is admitted into evidence.)

THE COURT: Mr. Peterka, I don't believe you moved Dr. Banakar's CV in. If you don't want it in?

MR. PETERKA: That's a fair point.

THE COURT: All the others are in. And I am just wondering, do you want it in?

MR. PETERKA: I do. Thank you, Your Honor. Can I move Dr. Banakar's CV, which I think is DTX-3, can I move it into evidence, please.

MR. HAUG: No objection.

THE COURT: It's admitted without objection.

(DTX-3 is admitted into evidence.)

BY MR. PETERKA:

Q. Did you hear Dr. Hollingsworth testify earlier in this case?

A. Yes, I did.

Q. And do you agree with the opinions he expressed?

A. Yes, I do.

MR. PETERKA: Can I go to slide 14, now? I am sorry. Yes.

BY MR. PETERKA:

Q. I'd like to talk a little bit about the Doctrine of Equivalents. Are you familiar with the function-way-result test?

A. Yes, I am.

Q. How does that work?

A. In layman's terms, the substituted element performs substantially the same function in substantially the same way to achieve substantially the same result for the element.

Q. In your opinion, is the magnesium stearate in the Zydus ANDA product an equivalent of the excipient with melting points below 90 degrees C that are listed in part (a) of claim 1?

A. In my opinion, the magnesium stearate used here is not equivalent of substance that melts below 90 degrees Celsius.

MR. PETERKA: Can we go to the next slide.

BY MR. PETERKA:

Q. What does the '720 patent teach about the way in which the claimed lipophilic meltings below 90 degrees C work?

A. The '720 patent teaches that the low melting point

with low melting excipients soften and/or melt to incorporate the active ingredient by simple dispersion in that melt.

And then after the dispersion is cooled, after cooling at room temperature, that creates the inner matrix.

Q. Do other parts of the specification support your opinion?

A. Yes, they do.

MR. PETERKA: Can I have the next slide.

BY THE WITNESS:

A. There are several examples in the '720 patent that shows the low melting point excipients are heated to facilitate dispersion of the active ingredient, in this case, mesalamine, in a lipophilic matrix.

If we go through the slide, there are four examples.

Example 1, top left box, the drug, the two excipients that are lipophilic are carnauba wax and stearic acid. With heating, they will melt and form and provide a volume for the drug to be dispersed in it, to result in a homogeneous dispersion when cooled that will give the structure to the matrix.

The same thing with Example 2. Same excipients, lipophilic, carnauba wax and stearic acid, on heating.

Example 3, another excipient, lipophilic

excipient, beeswax and palmitic acid, with heating, the drug, homogeneous dispersion, giving the structure on cooling.

Example 5, again carnauba wax and stearic acid, heating, resulting in homogeneous dispersion after the drug is added to it. And on cooling, it provides the structure.

MR. PETERKA: And just for the record, that is Examples 1, 2, 3, and 5 of the '720 patent.

Let's go to the previous slide.

BY MR. PETERKA:

Q. That is the patent there, DDX-10.15 and that is from the '720 patent, column 2, lines 48 through 59.

A. That is correct.

MR. PETERKA: Can I go to the slide 17.

BY MR. PETERKA:

Q. So, in your opinion, does the magnesium stearate in the Zydus ANDA product function in the same way as the substances that melt below 90 degrees Celsius that are described in the patent?

A. No, the magnesium stearate in Zydus ANDA product is not equivalent to the substance melting below 90, but substance melting about 130 degrees is not equivalent to a melting point below 90 degrees.

Secondly, the magnesium stearate does not function in the same way as the claimed lipophilic

excipients that melt below 90 degrees and produce an environment to facilitate the dispersion of mesalamine into a matrix structure.

Q. Do you agree with Dr. Sinko that magnesium stearate in the Zydus ANDA product functions to control the release of active ingredient?

A. No, I do not agree that the magnesium stearate in Zydus's product controls the dissolution of the release of the drug. And we're to talk about that later in my testimony in detail. And I have seen no evidence to that effect either.

MR. PETERKA: Could I have slide 18.

Moving on here to the next point, I'd like to talk about the requirement of the claimed matrix consists the substances consisting of the materials listed in part (a) of claim 1.

Can I have the next slide, please.

BY MR. PETERKA:

Q. Dr. Banakar, have you analyzed how Zydus makes its product in coming to your opinions that we're talking about today?

A. Yes, I have done that.

Q. And what is shown on this slide? This is DDX-10.19.

A. DDX-10.19, I put together the manufacturing overview of Zydus's ANDA product, and how they process it to get to

the formulation of the product itself.

First step in the process is compaction. The components of that compaction are provided just below that. Those components are then compacted.

And that compact is further sized.

The sizing will give those small compacts, which are then granulated, wet granulated.

The granules are dried.

The dried granules are then lubricated with magnesium stearate which form the precompression blend because they are to prepare tablets out of it.

So then these, this precompression blend will be compressed into tablets.

Then the resulting tablets are coated with functional coats. And.

Then, finally, they are coated with a film coat. That is their final dosage form.

Q. And the information on this slide is from DTX-17 and DTX-18. Can we just turn to those documents real quick in your booklet?

A. Yes.

Q. We already looked at DTX-18. Did we look at DTX-17, though? Can you take a look at that?

A. (Witness complies.) Yes.

Q. And what is DTX-17?

A. DTX-17 is the quality overall summary, the title page of the quality overall summary of Zydus's ANDA product.

MR. PETERKA: Can I go back to the slide, please?

So I don't believe DTX-17 is in. I'll move it into evidence. Defendants would offer it into evidence, if there is no objection.

MR. HAUG: No objection to DTX-17.

THE COURT: Admitted without objection.

(DTX-17 is admitted into evidence.)

BY MR. PETERKA:

Q. And just for the record, the information on this slide that you were just talking about on DDX-10.19 is from DTX-17 at ZYDUS_MES23436, and then again at 23458 through 60, and 23462, and then also from DTX-18 at ZYDUS_MES0235660-61?

A. That is correct.

Q. Is there any particular step in the manufacturing process that you are going to focus on today in connection with your noninfringement opinions?

A. The step that I am going to focus on is the first one, which is the compaction step.

Q. Can you explain what the compaction step is in the Zydus ANDA product?

A. Compaction step in general is we have a blend of dry powders which contains one or more ingredients. And that

blend is then compacted through the compaction with a machine known as a roller compactor. It was originally known as a Chilsonator but now it is known as a roller compactor.

THE COURT: Can you repeat that, what it was formerly known as?

THE WITNESS: Chilsonator. C-h-i-l-s-o-n-a-t-e-r, or o-r.

THE COURT: Thank you.

MR. PETERKA: Can we go to the next slide while we're at it.

THE WITNESS: Yes.

BY MR. PETERKA:

Q. All right. Continue. Thanks.

A. This is the schematic representation of a roller compactor from a reference, from the reference which is on the left-hand side of the slide.

This is from the article authored by Miguelez.

MR. PETERKA: Can you blow up the reference on the top left, please?

BY THE WITNESS:

A. That is the journal, International Journal of Pharmaceutics, and the title of the publication is The Effect of Lubrication on Density Distribution of Roller Compacted Ribbons.

Authors are Miguelez-Moran, Wu, and Seville.

Q. And is the International Journal of Pharmaceutics a reputable journal?

A. Yes, it is.

Q. Do you consider it to be a reliable authority?

A. Yes, it is.

MR. PETERKA: Can I go back to the slide, please.

BY MR. PETERKA:

Q. So I think you were in the process of explaining roller compaction?

A. Yes. Well, there is material which is to be compacted which is usually a fluffy material which is high density, which means that one gram of drug requires a lot of volume.

So if I have 1,200 milligrams of drug which is to be administered in a dose, it would be too large for a patient to consume or swallow. So it will be compacted so the particles will be smaller. The particles of the compacts will be larger particles, and that is what this machine does.

Q. Doctor, I think you said just before you do it for API that has a high bulk density.

A. That is correct. The bulk density is low where the one gram of drug requires a large volume, so it would be low.

Now, that material is then compacted with the

two rollers. They rotate in opposite directions. The distance between these two rollers is adjusted to get the thickness of the ribbon you want.

The powder material is processed through this. It moves through this, and gets compacted.

And the result is a ribbon or a sheet of material that comes out of it which is further processed to granules.

Q. Is roller compaction a common procedure in manufacturing pharmaceuticals?

A. Yes, it is a very common procedure. It has been used for 30-40 years as of today.

Q. Have you ever used roller compaction?

A. Yes, I use it very routinely as a matter of fact. I just used it a month ago.

Q. Do you know why Zydus roller compacts mesalamine in its ANDA product manufacturing process?

A. Yes, I do.

Let's go to the next slide, please.

Zydus composition is compacted in the first step, has three components to it, three ingredients: mesalamine, colloidal silicon dioxide, and magnesium stearate.

The important part, one of the important part is mesalamine, the dose is 1,200 milligrams, a large dose, as I

was talking about. And it is very fluffy material. So I need to compact it so that I can bring the size of the final dosage form reasonable for the patient to swallow. And that is the reason why it is compacted.

So this composition is first put together and blended where the silicon dioxide, colloidal silicon dioxide acts as a glidant. Glidant is basically an ingredient which moves the material from one place to the other easily.

Then there is also lubricant added. The function of the lubricant is to ensure the material doesn't stick to the rollers or anything as it is moving because if it does, then it can jam the equipment, and if it happen numerous times, that can lead to basically the breaking of those cylinders and ruining the whole process. So that is the reason why lubricant is added.

Now, this composition is blended and then passed through the roller compactor together, to compact.

To give you an idea about the composition itself and in the perspective of the mass, there is 1,200 milligrams of the drug in the tablet, 5 milligrams of colloidal silicon dioxide, and 4 milligrams of magnesium stearate. So the total mass for the tablet is 1,209 milligrams.

Putting it into perspective. If each milligram is represented at one dot, there are 1,200 dots. There are 4 dots for magnesium stearate and 5 dots for colloidal

silicon dioxide. That is the composition that is compacted.

Q. Thank you.

MR. PETERKA: Can I just go back to the previous slide.

And I would, defendants would like to move into evidence Figure 1 out of the Miguelez reference, which is Figure 1 of DTX-23. If it's allowed into evidence I, would call it, I'll call it DTX-23.A.

MR. HAUG: No objection.

THE COURT: It is admitted without objection.

(DTX-23.A is admitted into evidence.)

MR. PETERKA: Could I go back to slide 19?

BY MR. PETERKA:

Q. So Dr. Banakar, after the compaction step, what happens in the Zydus manufacturing process? Just briefly because we heard about this already.

A. You compact the size to small compacts. Then it is mixed with other ingredients. In this case, the important ingredient is sodium carboxymethylcellulose, which is the release controlling ingredient, along with other ingredients, and that is wet granulated.

The wet granulation is then dried.

The dried granules are then lubricated with magnesium stearate and a filler, the microcrystalline cellulose and a glidant.

So that is then compressed through a tableting machine, and the compressed tablet will be the result of that compression.

Those tablets are then coated with functional coats, and then finally film coated, which will give the final dose and form.

MR. PETERKA: Can go back to slide 21, please?

I think this is the slide we were just looking at.

BY MR. PETERKA:

Q. Now, you heard Dr. Sinko testify on Tuesday I think that in his view the roller compaction step produces granules containing colloidal silicon dioxide and magnesium stearate. Did you hear that?

A. Yes, I did.

Q. Assuming for the sake of argument the compaction step in the Zydus ANDA product produces granules that are macroscopically homogeneous structures in all their volume, what would those structures consist of?

A. Subsequent to or the result of the compaction would produce structures or so-called granules which were primarily, which will be of mesalamine or mesalazine in which there will be colloidal silicon dioxide and magnesium stearate put in it.

Q. And what would be the rough percentages of the three

ingredients you just mentioned in the material that comes out of the roller compaction step in the Zydus ANDA product?

A. 99.26 percent is mesalamine, .41 percent is colloidal silicon dioxide, and .33 percent is magnesium stearate.

MR. PETERKA: Can I go to the next slide, please?

BY MR. PETERKA:

Q. So looking at the list of materials in part (a) of claim 1, does colloidal silicon dioxide appear in that list of materials.

A. No, it does not.

Q. If there is a macroscopically homogeneous structure in all its volume form in Zydus's compaction step, is the colloidal silica unrelated to that element?

A. No, it cannot be unrelated because as I just said, if that so-called structure is formed, it will be the structure of mesalamine in which colloidal silicon dioxide will be dispersed in it, so it cannot be unrelated. It is part of the structure.

Q. Does the '720 patent describe any lipophilic matrices having colloidal silicon dioxide?

A. Yes it does.

MR. PETERKA: Can we go to the next slide?

BY MR. PETERKA:

Q. What does it say about it?

A. Column 1, lines 42 to 47 of U.S. patent '720, in the section on background of the invention, the prior art teaches colloidal silicon dioxide can be a part of the inert matrix. The colloidal silicon dioxide does the porization or form the pore for the inner lipophilic inner matrix which will have access to water or the fluid which otherwise it would not have. And that is where colloidal silicon dioxide does the porization of that lipophilic content matrix.

Q. And how does this support your opinion that colloidal silicon dioxide is part of any macroscopically homogeneous structure in all its volume that results from the Zydus compaction step?

A. In the compaction step, what I see is, it is going to be particularly mesalamine in which colloidal silicon dioxide will get dispersed. Colloidal silicon dioxide is hydrophilic, and it will be hydrophilic or that will be in that compact.

MR. PETERKA: If I can go back to the previous slide. Actually, slide 21.

BY MR. PETERKA:

Q. Just for the record, the information that you were reading for the amount of ingredients in the compaction step, that is from DTX-17, ZYDUS-MES 23436?

A. That is correct.

Q. Back to the description of the porization. How does

the porization element work?

A. As I said, the porization element works in providing access to fluids which otherwise it would not for the inner lipophilic matrix aspect of the '720 patent.

Q. Does a material have to swell upon contact with water to be considered hydrophilic under the Court's claim construction?

A. Hydrophilic, the claim construction from the Court has come down as "hydrophilic" means "affinity for water." It has nothing to do with as or say anything about swelling or not.

Q. In your opinion, if there is a macroscopically homogeneous structure in all its volume formed from Zydus's compaction step, the roller compaction step, is silicon dioxide an impurity in that structure?

A. No, it cannot be an impurity because it is intentionally added for a certain function. It cannot be impure.

MR. PETERKA: I'd like to move on. Can I have the next slide, please.

BY MR. PETERKA:

Q. I'd like to move on to talk a little bit about the matrix structure. Specifically, your opinion on this slide, what does this slide say?

A. The slide says: Magnesium stearate in the Zydus ANDA

product is not "a macroscopically homogeneous structure in all its volume." For that, you will need to know what exactly is this matrix.

Q. And can you provide an example of what a matrix is as that term has been construed in this case, which is "a macroscopically homogeneous structure in all its volume?"

Go to the next slide.

BY THE WITNESS:

A. Yes. While prosecuting the '720 patent, the patentees provided numerous literature information in order to define or make the Examiner understand what is a matrix.

This is one of the reference. The first reference is Martin's Physical Pharmacy reference where "matrix" is defined as monolithic or monolith. It refers to it as "a single mass or block of material." And that defines, monolithic device refers to a rate-controlling polymer matrix throughout which the drug is dissolved or dispersed.

In the next slide, there is a little bit more explanation and illustration where this is originally illustration. This is a clean copy of it, where it says monolithic is the matrix.

So this is the polymer matrix in which the drug is uniformly dispersed, thus forming the monolith or the structure. So that is structure we see. That is from this

same reference in a little more detail. DDX-10.26.

Continuing on, next slide, please.

The second reference I provided was --

THE COURT: Did we have a reference? It may have been on there, Doctor, and I just missed it, that last slide.

MR. PETERKA: Yes, I was going to go back and clear it up. Do you want me to do it now?

THE COURT: Yes, sure.

MR. PETERKA: Can I go to slide DDX-10.25.

This is from the Martin's Physical Pharmacy reference that Dr. Banakar mentioned. This is in DTX-2 which is the prosecution history at PLMESA03534294. And I don't believe DTX-2 is in evidence yet.

Defendants would offer DTX-2 into evidence.

MR. HAUG: No objection.

THE COURT: All right. Admitted without objection.

(DTX-2 is admitted into evidence.)

MR. PETERKA: Then can I go to the next slide right now.

BY MR. PETERKA:

Q. This is the illustration you were just talking about; right, Dr. Banakar?

A. Yes.

Q. This is also from the Martin's Physical Pharmacy text?
A. That is correct.
Q. This appears, on the left I think we have the actual copy from the prosecution history; is that right?
A. That is correct.
Q. On the right I think is a cleaner copy.
MR. PETERKA: The one on the left is actually from DTX-2 at PLMESA03534295.
The cleaner version from Martin's itself is cited as DTX-13, page 516.
And if I would be allowed, defendants would move into evidence the image on the right-hand side of DDX-10.26 from the Martin's Physical Pharmacy book as DDX-10.26A.
MR. HAUG: No objection.
THE COURT: All right. It is admitted without objection.
MR. PETERKA: Thanks, Your Honor.
(DTX-13A is admitted into evidence.)
BY MR. PETERKA:
Q. All right. Dr. Banakar, I think you were moving through these slides here.
A. Yes. The next one is the reference that the patentees provided was another reference, Modern Pharmaceutics, where again what we see is the drug dispersed

in this polymer matrix, and thus a matrix is created where the drug is dispersed into the polymer.

And when present matrix is put into a medium where the drug starts to dissolve out of it, after it is put into the medium at time zero, as time progresses the drug dissolves out of the matrix, and then at some time point, if you want to look at it, what we see is part of the matrix has the drug gone, which is dissolved out of it, and some of it remaining.

Thus, we can see the ghost or the skeletal, skeleton of the matrix. So that is it, that is the matrix that we should see, and the drug continues to dissolve out of it. Numerous terminology have been used, those terminologies include a polymer ghost or a skeleton or a honeycomb. All of those mean the same thing, same thing where the structure has lost the drug which originally was formed with the dispersion.

Q. And just to clear the record up -- I am sorry. Were you done? Go ahead.

A. No.

THE COURT: Well, actually you know what? It's a good idea if it he does it for the record because you are talking about something which could go on now for some pages in the transcript where I am not going to know. I am not going to know where this is, going back and looking, unless

you put it into the record.

MR. PETERKA: Right, I'll do it at the beginning from now on.

THE COURT: That will help.

MR. PETERKA: We have on DDX-10.27, this is two images. The one on the left -- and, Dr. Banakar, please keep your train of thought.

THE WITNESS: Yes.

MR. PETERKA: I have to interrupt you here for a second.

The one on the left is from DTX-2. It's at PLMESA035334283-84. It's an excerpt from the prosecution history to text. On the very top, there is a cutoff from the prosecution history. Under that, I believe somebody wrote it to be a little more legible, and below that, the third box on the left-hand side of the slide, is the image that is on those pages of the prosecution history.

The image that is on the left is from Modern Pharmaceutics.

On the right-hand side, we have again a cleaner copy so the Court can actually see better what is going on there. And that is Figure 7 from Modern Pharmaceutics, which is DTX-31 at page 587.

Defendants would move into evidence that image on the right-hand side of DDX-10.27 as Exhibit DTX-31A, if

there is no objection.

MR. HAUG: No objection.

THE COURT: All right.

MR. PETERKA: Just to --

THE COURT: Admitted without objection.

(DTX-31A is admitted into evidence.)

MR. PETERKA: Thanks, Your Honor.

And just to back up one second. I am told I misnumbered the last exhibit. The image on the right-hand side of DDX-10.26 should actually be DTX-13A.

THE COURT: I'll ask you all to make sure you have that cleaned up for the record.

MR. PETERKA: Thanks Your Honor.

BY MR. PETERKA:

Q. All right. Go back to DTX-27. I think we were still on this one, right?

A. Yes.

Q. All right.

A. Just to summarize and to deal with that.

This is Figure 7 which is cleaned up here and, as I say, Figure 7. Matrix devices, that is a matrix device, as the name implies, consists of drug dispersed homogeneously throughout a polymer matrix, as represented here.

And that was the representation of the polymer

matrix here and how it works.

Next slide, please.

Q. All right. Just let me stop you there and clear this up.

MR. PETERKA: This is DDX-10.28. And this is another excerpt from the DTX-2 in the prosecution history at PLMESA03534309.

This is a translation of an Italian reference, Il Prodotto Chimico submitted by Cosmo during the prosecution history.

And defendants would offer into evidence -- well, it's already in. We don't need to.

THE COURT: All right. Go ahead.

BY MR. PETERKA:

Q. Go ahead, Dr. Banakar.

A. This is the third reference that the patentees provided which is from Il Prodotto Chimico where it is an Italian journal. It has been translated.

They have defined "matrix systems."

They are commonly known as those therapeutic devices where the drug is uniformly dispersed in the whole body made of polymeric material. That is how the matrix is.

MR. PETERKA: Can we have slide 29, please?

BY MR. PETERKA:

Q. Have you seen any evidence in this case that the

magnesium stearate in the amount present in the Zydus roller compaction step formed a macroscopically homogeneous structure in all its volume?

A. No, I have not seen any evidence to that effect. Also, looking at the comparative picture here, as I said in perspective, we have this much amount of magnesium stearate which has to be dispersed to get that inner lipophilic matrix. Is very unlikely that is what would happen, in which the drug mesalamine is dispersed in it.

Q. So actually I may have misstated something. I want to make sure it's clear.

With respect to the material coming out of the roller compaction step, the compaction step in the Zydus ANDA product process, have you seen any evidence in this case that the magnesium stearate in the amount present in that material forms a macroscopically homogeneous structure in all its volume?

A. No, I have not seen that.

Q. And if there is a structure that is, or a macroscopically homogeneous structure that is produced from that step, in your opinion, what does it consist of?

A. As I said earlier, the structure that would be created after the material has gone through the compaction step would be basically mesalamine compacted with colloidal silicon dioxide and magnesium stearate would be dispersed in

it.

MR. PETERKA: Could I go to the next slide?

BY MR. PETERKA:

Q. I want to move on to your next point. What is on this slide?

A. This is another reason or another rationale provided where mesalamine is not dispersed in "a macroscopically homogeneous structure in all its volume" consisting of magnesium stearate.

Q. So have you seen any evidence that the mesalamine -- let me strike that and back up.

With respect to the material formed from the compaction step in the Zydus ANDA product, have you seen any evidence that mesalamine is dispersed in a "macroscopically homogeneous structure in all its volume" consisting of magnesium stearate?

We can go to the next slide.

A. No, I have not seen evidence to that effect.

Let's look at what is dispersed. "Dispersed" is defined or construed as "sufficiently mixed to incorporate one substance into another."

We are looking at '720 patent. It says: wherein the active ingredient mesalamine is dispersed ... in said lipophilic matrix.

So there is reason I have said that mesalamine

is not dispersed in such a lipophilic matrix made of magnesium stearate.

THE COURT: Okay. And Mr. Peterka, this is goes for both sides, but it will be a real help to me if right at the get-go, instead of saying next slide, you will say DDX-10.31, and that way I you know when I will look at the record this is what was on the screen and the witness on the stand was talking about it. That will be an assist.

MR. PETERKA: I apologize, Your Honor.

THE COURT: That's fine. Go ahead.

MR. PETERKA: This is slide DDX-10.31.

Can I have slide DDX-10.32?

BY MR. PETERKA:

Q. I want to move on to your next point. What is that?

A. The next point is the alleged "inner lipophilic matrix" does not "exhibit lipophilic properties" in Zydus's ANDA product. Therefore, it does not infringe.

Q. What is your understanding of the meaning of the term "lipophilic" as it relates to the claims?

THE WITNESS: Can I go to the next slide, DDX-10.33.

By THE WITNESS:

A. The term "lipophilic" is construed as "poor affinity towards aqueous fluids.

"Hydrophilic" is construed "has an affinity for

water." And,

"Inner lipophilic matrix" is "a matrix that exhibits lipophilic properties and is separate from the outer hydrophilic matrix."

I have reviewed the report as well as I heard Dr. Bellantone's testimony yesterday, and I agree with him that Dr. Hoag's results do not show a matrix with lipophilic properties.

Q. So in your opinion, would the compacted mesalamine in the Zydus ANDA product exhibit lipophilic properties?

A. In my opinion, they will not provide lipophilic properties.

Q. Is there anything about composition of the compacted mesalamine that supports your opinion that it does not exhibit lipophilic properties?

A. When you look at the composition, it has mesalamine and colloidal silicon dioxide as well.

MR. PETERKA: Can we go back to slide DDX-10.29.

BY THE WITNESS:

A. The composition of the compact is mesalamine, colloidal silicon dioxide, and magnesium stearate.

Colloidal silicon dioxide is hydrophilic. Mesalamine is also hydrophilic with respect to this composition. And the compact will be mostly mesalamine, so the property of such a compact will be hydrophilic.

Q. We talked about colloidal silica a little earlier. And I believe you said earlier that in your opinion, colloidal silica is hydrophilic?

A. That is correct.

Q. Are there any additional references that support your opinion that colloidal silicon dioxide is hydrophilic?

MR. PETERKA: And can I have slide DDX-10.37.

I'm sorry. Go back one side. Thank you.

THE WITNESS: I think the slide is wrong. It should be 10.34.

MR. PETERKA: 10.34. Thank you.

BY THE WITNESS:

A. Colloidal silicon dioxide here is this reference in the Handbook of Pharmaceutical Excipients.

Colloidal silicon dioxide is an excipient which is monograph in this textbook of Handbook of Pharmaceutical Excipients.

If we look at what it says, it is hygroscopic. That means it attracts water, so it has an affinity for water, and it absorbs water in large quantities without liquifying.

MR. PETERKA: Just for the record, this is DTX-33 at pages 143 and 145.

BY MR. PETERKA:

Q. This is from the Handbook of Pharmaceutical Excipients, Third Edition. Dr. Banakar, do you consider this to be a reliable source?

A. Yes, very reliable source because formulators go to this source all the time to select excipients for their composition.

Q. This is the excerpt from the handbook for colloidal silicon dioxide. Can you read just what is on that excerpt?

THE COURT: He just did. That's enough for me.

MR. PETERKA: Okay. Thanks, Your Honor.

Dylan can you put up DTX-17, please?

Can I go to page 23425?

BY MR. PETERKA:

Q. And, Dr. Banakar, can you please turn to DTX-17 in your book?

A. Yes.

Q. What about mesalamine? Can you tell me, I think you mentioned earlier it was hydrophilic.

A. Yes, I did. What we see on the slide is mesalamine and its solubility measurement or it's the experimentation that Zydus did in order to determine the solubility.

These are various aqueous media in which solubility was measured. And it clearly showed that it is soluble in these media, so it is hydrophilic, and it also states here it is soluble, slightly soluble in water.

Q. Can you turn to DTX-35 as well?
A. (Witness complies.)
Q. What is this document?
A. DTX-35 is the Quality Control Department Certificate of Analysis for mesalamine product of the compound itself.

We look at the second test that is done to establish the quality of the mesalamine that is used. It says it is slightly soluble in water. And the results are, yes, is slightly soluble. So it is hydrophilic.

MR. PETERKA: Can I go back to the slide presentation?

And we can we go to DDX-10.35?

THE WITNESS: Yes.

MR. PETERKA: Let's back up a second.

So based on everything we discussed about the colloidal silica and the mesalamine -- actually, strike that.

Can we go to slide DDX-10.35.

BY MR. PETERKA:
Q. What are we going to talk about now?
A. See, the next reason for which noninfringement is what I believe is magnesium stearate functions as a lubricant in the Zydus ANDA product.
Q. And why do you say that?

MR. PETERKA: If you go to the next, DDX-10.36.

BY THE WITNESS:

A. Magnesium stearate in pharmaceutical formulations processing is universally known and accepted as a tablet lubricant. And this is the monograph for magnesium stearate in Handbook of Pharmaceutical Excipients. Monograph for magnesium stearate, it says it is well known lubricant.

But if you look at the functional category, it is a tablet lubricant that is used in .25 and 5 percent weight by weight in composition.

Q. And when are lubricants typically used in a manufacturing pharmaceuticals?

A. Lubricants are used when dry material or powders have to be moved from one part of the -- one step to the other step or one position to the other position in case of compaction. It is through the roller compactors.

If it is tableting during where the granules are then compressed and they are to be ejected out of that die, that is where we need a lubricant. Otherwise, they will jam the equipment. And that is where the function of lubricant is very essential.

Q. I think you mentioned this. You mentioned that includes roller compaction; right?

A. That was the first thing I said.

Q. Are other materials besides active ingredient lubricant typically used in roller compaction?

A. Yes. Other materials that are used are a glidant. And glidant, as I said earlier, it helps moving from one point to another point. That is where the glidant comes in where the material, dry material can move in a seamless effort, or effortlessly. Silicon dioxide is one glidant that is used in moving dry materials or powders.

Q. If you could turn in your book to DTX-23. This again this is the Miguelez article we looked at earlier.

A. (Witness complies.)

Q. And what does this article discuss in general?

A. Give me one second.

THE COURT: You know what? Why don't we do this? Let's go off the clock. We'll go on my clock now. I want to get some logistical things with you.

Doctor, you can go ahead and step down, if you would like. We're going to take a lunch break here at this point, okay? Thanks.

It just seems like a reasonable breaking point. I want to make sure we're all on the same page.

What is your operating -- go ahead, Doctor.

(Dr. Banakar returns to the back of the courtroom.)

THE COURT: Each side is working on how many hours? What is your total number of hours per side?

MR. HAUG: 12 and-a-half.

THE COURT: Okay. So we're all on the same

page. I think you are going to want to check because I am not sure but I think you have about an hour to go. But you should make sure you are where you are, recognizing that you need to finish what your case is. And I don't know whether you feel like you need to save any time for cross-examination, if there is a rebuttal case. I don't know if there will be. But I don't want anybody caught by surprise, and I don't know whether there is a rebuttal case.

Are you planning a rebuttal case, Mr. Haug.

MR. HAUG: We haven't made a final decision, but if I do, it's not going to be very long.

THE COURT: Good enough. So what I am going to do then is recognize that you have some stuff. And we're not going to go too late into the afternoon, but that we need to wrap it.

Is an hour going to be enough for you folks to make the decisions you need to make to decide what you want to do, if I take a break for an hour? Are you going to be okay or do you want me to try to be a nice guy? Do you need an hour and-a-half? What do you need?

MR. PETERKA: For the lunch break?

THE COURT: Yes, that is what I am asking. I am taking a break now. And I expect that when we come back, it's going to be to the end. Right?

MR. PETERKA: Right.

THE COURT: So I am going to try to give you an opportunity. You can confer with each other right now -- I'll sit here quietly -- and decide whether you think you need more time. Because once we're back in, I expect we'll be in the mode where we're just taking it to the end.

MR. GAERTNER: In an abundance of caution, I think an hour and-a-half would be appreciated.

THE COURT: All right. That is fine with you, I am assuming, Mr. Haug?

MR. HAUG: No problem.

THE COURT: All right. Then I give you until 1:00 o'clock. We'll come back, and that ought to give us the afternoon.

MR. HAUG: 2:00 o'clock.

THE COURT: Excuse me. I scared you all. I meant 2:00 o'clock. To come back at 2:00 o'clock.

Yes, that would have been great. I'll give you until 2:00 o'clock. We'll be back and that will give you a chance to march it right through the end.

Okay. Thanks. We will be in recess.

(Luncheon recess taken.)

* * *

Afternoon Session 2:04 p.m.

THE COURT: Thanks. Please be seated, Doctor. Please be seated, ladies and gentlemen.

All right. Mr. Gaertner?

MR. GAERTNER: Oh, and I will ask Mr. Haug to step up. I know you just asked us to talk about a potential rebuttal case after this, and I did have a conversation with Mr. Haug about that. And do you want me to characterize it? I figured that I would let you do it so I don't misspeak, Mr. Haug.

THE COURT: All right.

MR. HAUG: Well, we currently don't intend to put on a rebuttal case.

THE COURT: All right.

MR. HAUG: Of something could happen in the next hour that I may ask permission, but other than that, no.

THE COURT: All right. Good enough. Thank you, Mr. Gaertner.

Thank you Mr. Haug.

MR. HAUG: Thank you.

THE COURT: Mr. Peterka, please continue with your examination.

MR. PETERKA: Thanks, Your Honor.

BY MR. PETERKA:

Q. Good afternoon. Before we left, we were talking about DTX-23. I want to move on from that, so we're not going to discuss that.

Dr. Banakar, can you put up slide, I don't know, 41. Keep going. Back. 38. All right. 40. Got it.

Dr. Banakar, moving on to your next point that magnesium stearate does not control release in the Zydus ANDA product. And I apologize if I speak faster now, but given Judge Jordan's prompt before lunch, I think he has kindly advised me I have a shorter period of time, so I want to move a little faster.

A. Okay.

Q. I will apologize in advance.

The next pointe, there's no magnesium stearate does not control the release of melamine.

In your opinion, do the experiments --

THE COURT: You can speak fast, but you're still going to have to speak slowly enough for the court reporter to actually take it down.

MR. PETERKA: That's correct. All right.

BY MR. PETERKA:

Q. All right. In your opinion, do the experiments Dr. Sinko discussed the other day when he was testifying, the Zydus experts, do they show the magnesium stearate controls release of the active ingredient in the Zydus ANDA product?

A. No, they did not.

MR. PETERKA: Can I see slide 41, please.

BY MR. PETERKA:

Q. Let's talk about the comparison of F044 and F 048. Do you recall that?

A. Yes.

Q. In your opinion, are the differences in dissolution between these two batches attributable to the addition of lubricant?

A. No, for a number of reasons. First of all, the formulations that are being considered or compared are formulation F044 and F048, F044 and F048.

Now, when you look at the composition that is disclosed in this table, you see F044 has compacted mesalamine at 1200 milligrams, and F048 has compacted mesalamine at 1,2O09 milligrams. This extra nine milligrams, it says here, contains nine milligrams of lubricant. And I heard him testify that these nine milligrams were nothing but magnesium stearate.

If you actually look at the composition, the composition which is stated here, the same thing here that I see, it has Aerosil as well, it is three milligrams, and magnesium stearate, six milligrams. So this amounts to nine, so this is not only magnesium stearate. That is one difference.

Q. And just can I just stop you there? Can we go look at those lab notebooks real quick?

A. Okay.

MR. PETERKA: Can I have DTX-37, please, at 54352. All right.

BY MR. PETERKA:

Q. Do you see, Dr. Banakar, this is the lab notebook page with F048 on it.

A. That is the formulation.

Q. Okay?

A. Yes.

MR. PETERKA: Go to the previous page.

BY MR. PETERKA:

Q. This is the actual formulation for that batch; is that correct?

A. Yes.

Q. Sorry.

THE COURT: What exhibit number are we looking at?

MR. PETERKA: This is DTX-37.

THE COURT: Thank you.

THE WITNESS: The mesalamine, compacted mesalamine, is from F046, that is correct.

Q. Can we see the formulation for F046?

A. The F046 formulation has three milligrams of colloidal silicon dioxide or Aerosil 200, and magnesium stearate, six milligrams. That is nine milligrams in total.

Q. Thank you. And that's at DTX-37 at 54348. And F048,

what page was that at? 52?

And defendants would move evidence into DTX-37.

MR. HAUG: No objection, Your Honor.

THE COURT: It's admitted.

(DTX-37 Exhibit was admitted into evidence.)

THE COURT: I don't have much to do here, but I've got to say my part.

MR. PETERKA: I'm sorry, Your Honor.

THE COURT: It's admitted.

MR. PETERKA: Back to slide DTX-10.41.

BY MR. PETERKA:

Q. Now can you continue with your explanation?

A. That, the difference, not only magnesium stearate, also has Aerosil, which we already know is hydrophilic.

The second important difference is that sodium carboxy methylcellulose in F044, which is 35 milligrams. It's double to 70 milligrams per tablet. Now, sodium carboxymethylcellulose we know is the release retardant agent or control release agent.

So there is a significant difference here, double difference. So I would expect that the dissolution of the drug coming out in F044 is going to be faster compared to F048, because it has more of the release controlling agent. So therefore just the change in dissolution rate, change amount of lubricant is

inappropriate.

Q. Thank you, Dr. Banakar.

If we could talk now about Dr. Sinko's discussion of a batch F108 and EMM196.

MR. PETERKA: Could I get slide 43, please. And could you go to -- could you put up DTX-43 at 349763.

BY MR. PETERKA:

Q. Now, Dr. Banakar, this is a lab notebook page on which the formulation for batch 1, F108 appears?

A. That is correct.

Q. And what is F108?

A. That is the formulation that we are going to talk about, and it is from the development lab notebook where formulation is still being developed. And just to give you a little bit more information, this is a very small batch of 3,500 tablets.

THE COURT: How many tablets?

THE WITNESS: 3,500.

THE COURT: All right.

BY MR. PETERKA:

Q. And in comparison --

MR. PETERKA: Could I have DTX-18. No, that's it.

BY MR. PETERKA:

Q. How many tablets of EMM196 in a batch?

A. EMM196 is a formulation which is an ANDA batch or exhibit batch. It has 150,000 tablets, so it is over -- a lot. It is 500 versus 150,000, so it is over, what, 50 times? A very large batch size.

Q. So you prepared a very small batch or formulation batch?

A. That is one of the differences.

MR. PETERKA: Can you go back to slide 43 please, DTX-43.

And defendants would move into evidence DTX-43.

MR. HAUG: No objection, Your Honor.

THE COURT: It's admitted without objection.

(DTX-43 Exhibit was admitted into evidence.)

THE WITNESS: The second important difference is F108, the batch which was prepared in compaction. There is no compaction in this batch when this batch was prepared whereas the exhibit batch had compaction followed by granulation and the rest of steps.

That is a significant change which can influence the dissolution rate of these formulations, so I would expect that F108, which has no compaction, which we were using earlier, which would release the drug earlier. Therefore, it would dissolve faster. It was compacted back to the compacted drug, which is going to take time, and it will release slowly.

So while, in addition to the differences in small size versus commercial size, or exhibit batch, a difference in this significant -- significant difference in this procedure where one step is completely -- can influence the dissolution, performance of these two lots effectively. Therefore, once again, comparing dissolution on these two lots based on only changes in amount of magnesium stearate is inappropriate.

THE COURT: I don't understand. I want to ask you a question. Let me just ask real quick, Doctor. What does the batch size have to do with dissolution rates for an individual pill? Why does that make a difference?

THE WITNESS: When I make a batch size of, let's say every one tablet is ten milligrams, and if I make a batch of 2,000 tablets, then I need only 300 -- 30 grams, so small procedure. The details of the entire batch, what it will take.

THE COURT: So the mechanics of the machine used?

THE WITNESS: Correct.

THE COURT: I got you.

THE WITNESS: Correct. And the lab size will have laboratory equipment and affect dissolution and scale up.

THE COURT: Thank you.

MR. PETERKA: Could we go to, I think, the next slide.

BY MR. PETERKA:

Q. And could you explain to us, you said earlier that roller compaction or the compaction step may impact dissolution?

A. As I said before, that when material which is fluffy or it occupies a large volume is compacted, it becomes compacted. Therefore, the bulk density becomes harder. Once it becomes harder, the size is large, the total surface area is decreased. So the granules are prepared of smaller particles of powder, and granules have other important characteristics because if their surface area is less than that of the comparable volume of powder. So that is a compacted material. So I have larger size, smaller surface area and compacted.

Now had you go to the other consideration, where we look -- looking at dissolution of the drug from the dosage form and what factors affect that rate. Effective surface area. The smaller the particle size, the greater the surface area of a given amount of drug, such as one gram. Therefore, the dissolution rate will increase.

So now this one gram is in powder form, it will have small particles, larger surface area, greater dissolution rate. If the same one gram is compacted, size

will be large, surface area below.

Q. Thank you, Dr. Banakar.

I think you mentioned when you were talking about -- so just for the record, DTX-40, it was the first passage you read from was from DTX-41, which was Ansel's pharmaceutical dosage form. Is that a reliable source?

A. That is correct, it is.

Q. He read it into the record sufficiently I assume, Your Honor?

THE COURT: Yes.

BY MR. PETERKA:

Q. The second reference is "Modern Pharmaceutics," which is DTX-42 at page 129 and 131. The previous reference was from DTX-41 at 198 to 199.

And is "Modern Pharmaceutics" a reliable reference?

A. Yes.

Q. You mentioned when you were talking about the Ansel's reference, you mentioned something about a larger size. I wanted to make sure. Did you mean particles that have more weight?

A. That is correct. Therefore, when they're compacted, they have more weight.

Q. So in your opinion, the difference in dissolution rate between these two batches could be explained by the

fact that the EMM196 had compaction whereas F108 didn't?

A. That is correct.

Q. Thank you.

Can we go on, I want to talk a little bit the doctrine of equivalents.

MR. PETERKA: Can I go to slide -- and just for the record, we were on slide DDX-10.41. Can I have slide D DX10.46, please. Actually, slide 10.53.

BY MR. PETERKA:

Q. We talked about the doctrine of equivalents a little bit earlier. Focusing on the yellow highlighting in this slide, what does the '720 patent teach about the inner lipophilic matrix and how it works?

A. The '720 patent talks about two matrices, a lipophilic matrix and then outer hydrophilic matrix. For our exhibit and understanding, I have used two colors to differentiate how each of the matrices work. The blue color is for outer hydrophilic matrix, and the yellow is for inner lipophilic matrix.

Imagine if you will the inner lipophilic matrix and outer hydrophilic matrix. When this composition is placed in water or fluid, where it starts to dissolve, the outer swells, and the swelling, outer swells, and the swelling hold the water from accessing the drug. Therefore, it continues to release. And at some point, it bursts open.

It bursts open, and then the lipophilic matrix is exposed from which the drug is going to be released by diffusion mechanism.

What diffusion mechanism is is a drug in that lipophilic matrix. It dissolves, and the dissolved drug comes out of that matrix, because diffusion transfers out in molecules from a matrix or surface or a film. There are two different mechanisms in mind. One is through swelling.

Q. Can we go to the next slide, DTX-10.54.

How does Zydus' ANDA product control the release lease of mesalamine?

A. 10.54 is the composition of the Zydus ANDA product. Their retarding agent, release retarding agent, is sodium carboxymethyl cellulose, sodium CMC it's also referred to it as. That is a hydrophilic matrix. That is one that is controlling the release of drug from Zydus' product.

Q. Just for the record this is from DTX-17 at Zydus 23436.

Going back to slide 46, please. Now, even assuming that the -- this is purely assuming that the compacted mesalamine blend did somehow slow release of mesalamine from the dosage form, would it do so in the same way as the claimed inner lipophilic matrix?

A. No, it will not do that, because even if you assume, first of all, there is no lipophilic matrix of magnesium stearate and the drug is dispersed, has to be dispersed in this matrix, the lipophilic matrix, and now we look at, how does the drug release control.

THE COURT: Well, don't skip over that diagram. I mean, you were in here, I assume, when Dr. Sinko was testifying?

THE WITNESS: Yes.

THE COURT: He spent some time, I was having a conversation with him, that the magnesium stearate forms a matrix. Right? I take it you disagree with that. I want you to explain to me why you disagree with that.

THE WITNESS: First of all, the lipophilic matrix that is defined is a matrix which is uniform throughout its volume, Homogeneous throughout its volume, and it has to have structure.

Now, there is no structure that I see, or that I have seen. There's no evidence to that effect, so there is no matrix that is formed that I believe has been proven.

Number two is, if you look at the context of it, the so-called compaction is considered as the so-called inner compact or matrix, then 99 percent, a substantial amount, is drug which is hydrophilic. Colloidal silicon dioxide is also hydrophilic. Magnesium stearate is

dispersed in it. So I don't see any matrix there.

So now if you look at the Zydus product, it has carboxy methylcellulose, which is hydrophilic. You take it in water, it swells, and then it will -- I will show had you how does the drug --

THE COURT: I understand your point about the outer, that release return. I was just focused on this matrix, the asserted matrix structure that I'm hearing from the plaintiffs' Zydus and I understand your answer. Thank you.

Go ahead, Mr. Peterka.

MR. PETERKA: Thanks, Your Honor.

BY MR. PETERKA:

Q. Now, I would like to move on and cover another bit of the doctrine of equivalents.

MR. PETERKA: Can I go to slide 54.

BY MR. PETERKA:

Q. Does a product that utilizes for release, Zydus product that utilizes the release controlling mechanism you just discussed, the sodium CMC, does that function in the same way as a product that uses the claimed inner lipophilic matrix and outer hydrophilic matrix?

A. No, it does not. The primary reasons, a number of reasons, but the reason that I can show you, the '720 patent requires two matrices. One is lipophilic and one is

hydrophilic. These are like day and night different.

One is resistant to water or one has an affinity for water. So now if I have these two matrices, then I should see that the differences in seeing the dissolution, the dissolution performance of the drug. You don't see that here.

What we see is from a single matrix, which is -- I'm going to show you that. It is a single matrix which is operating where the drug is releasing linearly over a period of time, and that is what we see.

MR. PETERKA: Could I have slide 55, please. Actually, yes. That's perfect.

BY MR. PETERKA:

Q. I think you just referenced the dissolution testing that Vivian Gray and Dr. Little talked about, I think it was Monday. Is that what you were talking about?

A. Yes.

Q. Okay. And I think you were talking about Dr. Little expressed an opinion that -- well, I don't need to cover that.

MR. PETERKA: Can I have -- can I have the title of this reference pulled up? This is DTX-64, by the way, at page 155.

BY MR. PETERKA:

Q. This is a journal article. What is this journal?

A. The journal is "Scientia Pharmaceuticals." The title of the article is "Factors Influencing Drug Dissolution Characteristic From Hydrophilic Polymer Matrix Tablet."

Q. And can you -- and do you consider this to be a reliable reference?

A. Yes, it is.

Q. You would consider it in your work?

A. Yes.

MR. PETERKA: Can I have back the slide DTX -- DDX-55.

BY MR. PETERKA:

Q. Now, you have a lot of experience with dissolution testing; right?

A. Yes.

Q. What are we seeing here? And I think we have an illustration, but you can start to explain it. Maybe we'll pull up the illustration as we go.

A. Forgive me. I'm going to give a little bit explanation on this. It will take a couple of minutes.

Q. Sure.

A. Imagine, if you will, if I have a tablet, which has hydrophilic matrix, and in that there is drug dispersing. That tablet is placed in water and you start the dissolution test, you run the dissolution testing.

Such a tablet, there are four of these. Now,

those are put into a dissolution test, and now what we do is, that tablet has a certain amount of drug that is going to dissolve out of it. So with time, we take samples, and then we collect the samples, analyze them and determine the amount of drug dissolved over a period of time.

We cumulatively add them, and that's how we get this, what's known as a dissolution profile. If this dissolution profile is linear, then that is what we see with hydrophilic matrices. They're linear. Y, it's the linear.

Q. Would you like -- oh.

A. I want to specifically focus on when all of these are hydrophilic matrices, all of these are linear, and I want to specifically focus on this profile, which is the profile generated from a hydrophilic matrix tablet. You see here hydroxyethyl cellulose. The hydrophilic matrix tablet.

When that is put into water, it will start to release the drug. There's a finite amount of drug that is released linearly up to a point and then it curves up a little bit. There's a reason for that. But what you see is, it is linear.

Why does it curve up? Because we are looking at more than 80 percent of the drug is dissolved, and after that, there is not enough drug maintaining to maintain this

rate. That's why we start to see the curve turning, and then if we reach a plateau where there is no more drug coming in, all the drug -- that matrix, the hydrophilic matrix.

Why am I going to concentrate on this? Because you see something like this in Gray's experiment.

Next slide, please.

MR. PETERKA: Before we move there, we're going to also offer into evidence Figure 3 of DTX-64, or move into evidence, so it will be DTX-64A.

MR. HAUG: No objection.

THE COURT: Admitted without objection.

(Exhibit was admitted into evidence.)

THE WITNESS: When we look at that figure and when you look at this figure, which is the dissolution start, here with the time -- yes. Put it in side by side. And we see at the time three hours where the dissolution is starting, same as zero times Y.

No drug dissolves in the first three hours, what she called it as pre-treatment where the outer does not dissolve. That's correct. So now everything from this point onward is similar to what we see linear. This is a hydrophilic matrix, which is giving a linear profile. This is also hydrophilic matrix, in my opinion, giving a linear profile. Why? Because the sodium carboxy

methylcellulose is a hydrophilic polymer in which the drug is inside.

Now, this also curves off, so that curving off is happening at around 80, 85 percent, so most of the drug is out. It cannot maintain this rate. And between this time and maximum, it is 100 percent dissolved. After that, there's no drug. There's a little bit slowing down because it cannot maintain this rate, and this is very, very normal for such a hydrophilic matrix. It's very normal. It's exactly what she saw.

And after that, there is no more drug coming in. This is just where the consequence here, because there is no more drug coming in. And the whole profile can be explained as a hydrophilic matrix within the drug over a period of time, which is also supported by pictures that she provided to us and those were discussed as well.

Q. Just for the record, you were comparing Part B from the figure, Figure 3 of this reference, which is DTX-64 that we just moved in. It's the figure to the right, the figure on the right. And you were looking at the one with the black triangles. I believe it's under that, in the legend B; is that right?

A. Yes.

Q. And you were comparing that to the dissolution curve from Ms. Gray's testing and Dr. Little, and I believe that's

PTX-900.1053; is that correct?

A. Yes.

Q. Thank you, Dr. Banakar.

What about Dr. Little's opinion that there's visual evidence of a second mechanism of release at work in Ms. Gray's study?

MR. PETERKA: If I could have slide 58, please.

THE WITNESS: What he was reporting was, well, there is release from this point and at 170 minutes, there's a slight change in the so-called profile in terms of how it is moving, and then hit goes to the maximum, and that goes off.

So this, he purported that that is an indication of the lipid, also called inner lipophilic matrix without analyzing whether there is magnesium stearate available.

Setting that aside, the real reason is not because the lipids are starting to operate. What he's seeing that it's 85 percent of the drug. What is left is ten percent over one hour, so it's going to slow down because it cannot maintain this rate. And the hydrophilic matrix is also disintegrating at the same time. So I have less drug, less matrix. It slows down, and that is why this so-called apparent change in the so-called factor moving linear can become a little slightly less.

MR. PETERKA: The next slide, please. Back up.

Sorry. DTX. Yes. And the graph you were just looking at was also PTX-900.1053. Can I have DDX-10.59, please.

BY MR. PETERKA:

Q. And what about the discussion or claim that there was visual evidence of a second release mechanism at work?

A. Right. So where look at this, he said the starting point, which is correct, three hours. That's the time when this tablet is now going to start to dissolve, because now you are in the right medium. It's in the right medium. The matrix is going to be hydrophilic matrix is going to be exposed.

Now 30 minutes en route. You start to see this has fallen. It's disintegrating, continuing on, will go for one hour, roughly one-and-a-half hours. 50 percent is gone, it starts loosening up more. All of the hydrophilic granules that are just disintegrating from the tablet continues on. It becomes smaller and smaller because it's disintegrating and dissolving.

Three hours now going forward. You see it getting further smaller. Almost close to four hours. Now we have very little of the tablet compact remaining, dissolving at the same time. Disintegrated granules are also disintegrating further and the drug is dissolving at four hours.

Very little of this humongous matrix is

remaining there, and at four hours, close to four hours, all of it is gone. 95 percent. Very little drug remaining. And the last point, we see -- the next one, please.

The last point we see is there is no drug, no matrix. So composite picture of the entire process. This is starting 13 minutes into the dissolution run. If I can imagine, this is zero time. Thirty minutes, one hour, continuing on almost four hours here. Ninety-five percent drug gone, five percent remaining. Now even at end of the dissolution run, so the plateau starts to occur. There is no drug. There is no matrix.

Q. Thank you, Dr. Banakar.

If I could just flip back to slide 59 so I get on the record the images you're looking at.

MR. PETERKA: Is this the first one? All right. All right.

So DDX-10.59, these are the picture of the tablets before dissolution. PTX-900.67. Is that right? And then the picture of the tablet at 12:56 p.m. is at 900.108.

Can I go to the next slide? The tablet at 1:56 p.m., PTX-900.184. Next slide, please. The tablet at 256 is 900.244. Next one. 317 is 900.255. And 900.269, that's at 3:47 p.m. And then WE have at 4:06 p.m., 900.281. 4:16, 900.282. And the reference for all of those is

900.67. These are all compiled on slide DDX 10.77. I think I think those are all in evidence. If they're not, we would move them in. I think they're in. Right?

Go to slide 67, please.

BY MR. PETERKA:

Q. Dr. Banakar, can you explain why there were fragments of the tablet floating throughout the media in the test?

A. I just gave a brief rundown. If you can please go to the previous slide, 10.65. 10.65, the composite picture.

Q. 10.66.

A. Sorry. 10.66. This process that you are utilizing. One is time. And the second is how the product is dissolving. And the third is how much it is dissolving over a period of time. You put that into perspective, and now go to 10.67, can be seen in this picture, the schematic, the dosage form, such as what we were talking about. It's disintegrating into granules. Granules are further disintegrating into fine particles.

And all along, all along, the drug is coming out, dissolving, and that is what we see. And what we are measuring is the amount of drug in this dissolution medium, or in this solution from time zero to infinity. And then infinity, we find that when all the drug from this tablet is gone and needs to get plateau and that plateau is at four hours. Roughly four hours.

Q. This is on slide DDX-10.67 and the schematic Dr. Banakar was just referencing was out of Ansel's pharmaceutical drug delivery system, DTX-41. I believe you already said that's a reliable reference; right?

A. Yes.

MR. PETERKA: And Figure 5.11. And defendants would move Figure 5.11 into evidence as DTX-41A.

MR. HAUG: No objection.

THE COURT: All right. It's admitted.

(Exhibit admitted into evidence.)

BY MR. PETERKA:

Q. Doctor Banakar I just want to touch on -- so, well, real quick. So in your opinion, the test results you've seen from Vivian Gray that we just talked about, those are consistent with, as I understand it correctly, those are consistent with a single hydrophilic matrix?

A. That's exactly what I believe.

MR. PETERKA: If we could go back to slide 49, please. I just want to touch on one last thing here.

BY MR. PETERKA:

Q. I wanted to talk about earlier you had on your slide about the requirement that active ingredients dispersed both in the lipophilic matrix and in the hydrophilic matrix.

Have you seen any evidence of any fines that are produced by the compaction step in the Zydus ANDA product

that are pure mesalamine?
A. No.
Q. Have you seen any evidence that there is mesalamine that's -- if Dr. Sinko is correct, if there is somehow a lipophilic matrix, that there is mesalamine that's separately in both an inner lipophilic matrix and an outer hydrophilic matrix in Zydus' ANDA product?
A. No, I don't see it.
Q. Are fines -- what are fines in your opinion? If you can explain them?
A. Fines are when I have a large composite, I'm slicing it, or if I'm making it smaller, I'm processing it. The entire composition becomes smaller and smaller, and you get the so-called distribution of area slices.

So a fine, I call it as miniature granules. So it is miniature, what we start off with and what we have.
Q. Would composition be the same?
A. That is what I expect.
Q. All right. Two quick sum-ups here.

So based on everything we've discussed today, what is your opinion as to whether the Zydus ANDA product infringes claim 1 of the '720 patent?
A. What I discussed today and what I have said over the last two hours is, it is my opinion that Zydus' product, Zydus' ANDA product does not infringe claim 1 or claim 3 of

patent '720 literally or under doctrine of equivalents.

Q. Thank you.

MR. PETERKA: And I don't have any other questions. Thanks.

THE COURT: Cross-examination, Mr. Haug.

MR. GEORGEK: May we approach the witness, Your Honor?

THE COURT: Yes, you may approach.

(Binders passed forward.)

THE COURT: Please proceed.

MR. HAUG: Thank you, Your Honor.

CROSS-EXAMINATION

BY MR. HAUG:

Q. Good afternoon, Dr. Banakar.

A. Good afternoon.

Q. I'd like to start by having you look at your slide DDX-10.2.

A. (Witness complies.)

Q. Did you prepare this slide?

A. Yes.

Q. I noticed in the slide, where you say Bachelor's Degree in Pharmaceutical Sciences, you don't have any schools listed where you went to school.

A. Oh. There was Bombay University in India. And that's it.

Q. That's it?
A. Oh. You want all of the schools?
Q. Well, I guess my question is why didn't you include your schools there?
A. I didn't think I needed it.
Q. I'd like you to go to DTX-3, please.
A. (Witness complies.)
Q. This is your CV; right?
A. That is correct.
Q. Now you may recall that Mr. Peterka maybe forgot to introduce the exhibit into evidence.
A. Yes.
Q. Is the CV accurate?
A. Yes.
Q. Up at the top, under your name, it says professor. Are you really a professor, a full-time professor?
A. No, I am not a full-time professor. I am full professor, and professor is an earned degree -- I am sorry -- earned rank, and that stays with you for life. And I know that very well because my dad was a full professor and he died as a professor as well.

But in that, that is a rank earned because of your scholarly activity and all the things you do to earn that rank, and that stays with you.

I am at other various academic institutions in

the world, and I have been recognized as a visiting professor.

Q. You are a visiting professor?

A. Correct, because I am not with them.

Q. Where it says universities listed, the first one listed is Massachusetts Institute of Technology (MIT). You never attended MIT, did you?

A. I attended MIT. As I said in my direct, that there was a focus, concentrated focused program in controlled release technology, advancements in control release technology, and that is what. That is where I earned a certificate. And that is a teaching thing, so I think that is relative.

Q. You never were awarded a degree of any kind from MIT, were you?

A. No, that was a certificate course.

Q. You attended a course you paid for five days; isn't that right?

A. No, I didn't have to pay for it because it is a course which is not available to everyone, at least in those years, where it was to be not only an indication but it also was recognized on the basis of why, if it would be allowed. So there was some criteria which was used. And I got a post-grant for advancement in a professional career, so that was the grant that paid for the course.

Q. Thank you, Dr. Banakar.

Now I'd like to ask you what you did to prepare for the opinions that you have given in this case. Do you recall when you were first retained as an expert in this case?

A. Honestly, no.

Q. Could it have been back in 2012?

A. Yes. This case has been so long. Yes, that is correct. That is possible.

Q. All right. Do you recall how many expert reports you have filed or served or prepared in this case?

A. I think five or six, but don't take me on that. It is between five and six, I think.

Q. Did you write all those reports yourself?

A. The way the reports were written were as it is done, there is discussions, there are onsite meetings, there is method meetings. And then the textual part comes out of it, which is discussed, and I approve it, and it goes through whether it meets the criteria of what I think is the way it is expressed is correct, and then that is how it comes out.

So, yes, I wrote it.

Q. Are you saying that the text report is drafted by the attorneys and then you review it and approve it? Is that what you are saying?

A. It is combination of both. Because technical matters

is where my expertise comes in as well as the language also comes in there.

The matter and the way it is to be structured, formatted, that all comes through the legalese. I can't do that.

Q. Thank you. Now, you have been sitting throughout this entire trial; isn't that correct?

A. Yes.

Q. You were here for the testimony of Mr. Kulkarni on behalf of Zydus; is that right?

A. Yes, I was.

Q. Have you ever met Mr. Kulkarni?

A. No.

Q. Have you ever spoken to him?

A. No.

Q. Have you ever been to Zydus in India where they manufacture this product?

A. No.

Q. So you have never seen the process itself; is that right?

A. I have a very extensive knowledge of all the equipment that is used. All the process that is being, that they undertake, I can attest to that.

So I can say that, yes, I have not physically been there, but I know the machine, compacting machine is

Cadmach, and the tableting machine is Cadmach. So I know that very well. So in that instance, yes, I know that. But when the product was being manufactured, I was not there.

Q. Did you ever read Mr. Kulkarni's deposition before this trial?

A. Way back, I may have. I don't know.

Q. Have you ever talked to any other Zydus formulators or scientists about how they manufacture their proposed generic version of this product?

A. No. And then once I am involved in the case, I can't talk to them anyway. So either way, I am not.

Q. Once you are involved in the case you can't talk to them? Why is that?

A. That is my understanding, because I should not talk about it.

Q. Have you done any testing in this case, Dr. Banakar?

A. Can you please define "testing?"

Q. Any kind of testing of the Zydus product in any way?

A. Other than looking at the ANDA, which is, that is a test, but other than that, physically no.

Q. Did you ever ask for any tests to be conducted to investigate any of the products of the Zydus product or process?

A. No, and I was not asked to do that either.

Q. Did you do any literature searching at all in coming to any of the opinions you have given in this case?

A. I don't know what you mean by "literature search." But the hydrophilic matrix, I have books and things in my own library which is, where I might have looked at it. That is the extent of it. But I am not asked to do this search with these terms, no.

Q. I'd like you to turn to Tab 1 in your book, in your binder. This is a copy of your deposition.

A. Yes.

Q. Okay. Your deposition was taken December 7th, 2014. Do you recall that?

A. Yes.

Q. And I'd like you to turn to page 52, please. Line 22.

A. Yes.

Q. "Question: Did you do any literature searches in coming to your opinions in this case?"

Go down to the answer, page 53, line 6.

"Answer: No."

Did I read that correctly?

A. Yes, that is exactly what I said.

Q. I'd like to move on to ask you some questions about infringement. It's a general topic. Okay?

A. (Nodding head.)

Q. You agree, do you not, that Zydus's ANDA product is a controlled release formulation?

A. Yes.
Q. You also agree that Zydus's ANDA product contains 5-amino-salycylic acid, also known as mesalamine?
A. That is correct.
Q. And the mesalamine in the proposed Zydus ANDA product is present above 80 percent by weight of the total composition; is that correct?
A. That's correct.
Q. And magnesium stearate is a salt of a hydrogenated fatty acid; isn't that correct?
A. That is correct.
Q. Do you agree that Zydus's ANDA product contains hydrophilic excipients?
A. Yes.
Q. The sodium starch glycolate used in Zydus's product is a starch derivative; isn't that correct?
A. That is correct.
Q. And, therefore, it is a 1(b) excipient as quoted for in the patent; isn't that correct?
A. That is correct. You are talking about a claim, I believe.
Q. Claim 1.
A. Okay.
Q. Claim 1(b). I am sorry.
A. That is correct.

Q. Thank you for the clarification. Do you agree that the hypromellose in Zydus's ANDA product is a hydroxyakyl cellulose?
A. That is correct.
Q. That is also a 1(b) excipient, is it not?
A. That is correct.
Q. And do you agree that the carboxymethylcellulose sodium salt in Zydus's ANDA product is as hydroxyakyl cellulose?
A. Sodium salt, that is correct.
Q. And that also a 1(b) element, is it not?
A. That is correct.
Q. And you agree that the hydrophilic materials in Zydus's ANDA product forms a hydrophilic matrix?
A. You will have to tell me what definition I have to use for "matrix."
Q. What is your understanding of what a "matrix" is as required by the '720 patent?
A. The way I understand it is it is asked for the definition, I am sorry, the construction that has come down. It says it has to be "macroscopically homogeneous in all its volume" and that is what I -- and it has to have structure. So that is how I look at a matrix in context of '720.
Q. I think you just said when you look at how it has come down, the claim construction for "matrix" is "a

macroscopically homogeneous structure in all its volume;" is that correct?

A. That is correct.

Q. That construction didn't come down from anywhere. Isn't that an agreed upon construction by the parties in this case?

A. Yes, that is word play. This is -- the way I understand anything being ruled is in the way of what has come down from the Court. So that's in that context.

Agreed upon is also correct because that is what it was mentioned in my slide 2 or 3, whichever slide it was.

Q. Within that claim construction of "a macroscopically homogeneous structure in all its volume," what is your understanding of the meaning of the word "structure?"

A. Structure to me is I have to have something that I can see as a structure. It cannot be something that is hanging in the air or it is just floating around. That is not a structure.

If you look at a good analogy would be if you look at a building where it was being built, you first put in the structure and then they put in all the various parts of the building. So the structure is there.

And I showed you where the structure was in my direct when I talked about "matrix" and where I have the drug dispersed in that structure. Where the drug goes out,

I see the structure left behind. So that tells me that, yes, this is a matrix.

Otherwise, I would not have accepted that it is a matrix in the term in the way '720 is defining it, or agreed upon definition.

Q. And I believe you testified that the structure is a monolithic structure; right?

A. Monolithic is one way they said it in that reference. And they have said monolithic equals matrix.

Q. Do you recall giving the opinion in your expert report that structure means monolithic?

A. That is exactly what I said, too. Monolithic.

Q. You remember giving that opinion, right?, or view?

A. It is possible, but I still believe monolithic is a structure, yes. You have the structure is as we saw in the slide that I showed you.

Q. Do you recall citing to a dictionary when you gave that definition of structure in your expert report?

A. I need to see it because I don't have it memorized right now.

Q. Can a structure, to your understanding, within the construction that we're talking about in the '720 patent, can that also be an arrangement of particles in a substance or body?

A. Not according to the way of '720 says. Because they

are not -- there is no structure. It is so-called hanging around.

Q. Sorry, Dr. Banakar. Just give me a moment.

All right. I'd like you to turn to tab 28 in your binder.

A. Yes.

Q. Okay. Do you recognize tab 28?

A. Sorry?

Q. Do you recognize this?

A. Yes. Merriam-Webster's Collegiate Dictionary.

Q. Do you remember referring to this dictionary in your expert report?

A. It is possible.

Q. Why don't we go to tab 2, paragraph 78 in your expert report.

Let me know when you are with me.

A. Yes, I am there.

Q. All right. Thank you. All right. We have paragraph 78. If we go to the bottom here, do you see, about two lines up -- one more. If we go to the top line there, it says "monolithic."

"Monolithic" means "cast as a single piece," or "consisting of or constituting a single unit."

And then it goes on: "(See Example S, Merriam-Webster's Collegiate Dictionary, 573 (10th Edition

1997)."

Did I read that correctly?

A. Yes.

Q. Now, going back to tab 28. Isn't that Merriam-Webster's Collegiate Dictionary that you were referring to in your expert report?

A. Oh, yes.

Q. And if you go to page 753 of the dictionary?

A. Yes.

Q. Upper right-hand corner, definition of monolithic. That is where you got this; right? Do you see where it says "2: Cast as a single piece."

It goes down below. "c: Consisting of or constituting a single unit."

That is where you got your definition that you put in your report; correct?

A. That is correct.

Q. All right. That is your definition for "monolithic" which you say is a structure within the context of this patent.

Why don't we go to page 1167 of the same dictionary. Next page over.

Let's look up the definition for structure. I'd like you to go to No. 4: "a: The arrangement of particles or parts in a substance or body."

Did I read that correctly?

A. The structure 4.

Q. I highlighted it on the screen.

A. Oh.

Q. Do you see that?

A. Yes, I see that.

Q. Okay. A short while ago, you said you didn't agree with that.

A. Correct. Because I still look at it in the context of '720. I need to see the structure. And structure as I look at it is polymer matrix. I need to see the drug dispersed in it, and that is what structure I need to see left behind.

Otherwise, just connecting two words from a dictionary does not constitute a definition of the meaning for the word.

Q. Let's go back to the patent, PTX-1. You can refer to it if you need to, but let me ask you a few questions.

Does the word "structure" appear in than patent claim, claim 1?

A. What is the number?

Q. PTX-1, it's the patent. Actually --

A. I don't have that.

Q. -- we have it up on the screen. I am just asking you about claim 1 of the patent. You are familiar with this

claim; right?

A. Oh, yeah. Yes.

Q. You would agree with me, right?, the word "structure" doesn't appear anywhere in that claim; right?

A. The way I understand it is that is the reason why there was a dispute and then it was agreed upon for the definition. So, yes, there is no word for "structure" explicitly stated there.

Q. Do you agree that the word "monolithic" doesn't appear anywhere in the patent claim?

A. That is correct.

Q. As a matter of fact, the word "monolithic" doesn't appear anywhere in the entire patent; is that right? Except the part that you may have referred to in the file history. I am only talking about the issued patent in the specification. Does the word "monolithic" appear anywhere in there?

A. The specification, then prosecution comes into that category, but if you are only talking about claim, no. Specification, prosecution, according to me, at least the way I understand it, is the prosecution information is also considered in the specification, but if you are talking about claim, correct, there is no word "monolithic" there.

Q. Okay. I was asking you before we got to the dictionary whether you agreed about certain elements of the

Zydus product. I'd like to go back to that.

Now, do you agree that the product of the roller compaction step in the Zydus ANDA process is uniformly dispersed in the hydrophilic matrix?

A. You must first tell me where the hydrophilic matrix is, and then I can tell you that, respond to that question.

Q. Do you think there is a -- do you know if there is a hydrophilic matrix coming in the product that comes out of the roller compaction step?

A. I said on a couple of occasions, and I say there, what we have that comes out after powder is compacted is mesalamine which is hydrophilic, colloidal silicon dioxide which is hydrophilic, so that compact is more than 99 percent hydrophilic.

Now, if that is put into the final dosage form you asked me, I just said that. That final dosage form is being like a single hydrophilic matrix. So there is your answer.

Q. So you are saying you do agree that the product of the roller compaction step in the ANDA process is uniformly dispersed in the hydrophilic matrix? Yes or no.

A. You must first tell me what "matrix" is.

Q. Why don't we turn to your deposition again. It's tab 1. This time, I would like you to go to page 258, line 12.

Are you with me?

A. Yes.

Q. Okay. I have it on the screen also.

"Question: All right. Given that description, would it be fair to say that the downsized compact pieces are dispersed within the hydrophilic materials that form the hydrophilic matrix in the Zydus product; correct?"

After an objection.

"Answer: Processing-wise, strictly they will be uniformly dispersed. But will they kind of connect to each other, no, because just the mass differences is fairly large. But, yes, it is required for uniform distribution because the content uniformities are stepwise in process quality control check, otherwise, you'd have problem with the product."

Did I read that correctly?

A. That is correct.

Q. Do you agree that the products that went into the Zydus roller compaction step, which is mesalamine, colloidal silicon dioxide and magnesium stearate, are all blended to uniformity before compaction?

A. That is the requirement for GMP, good manufacturing practices, and that is what I expect unless I see evidence otherwise.

Q. So you agree that that is what happens in the Zydus

product as it goes through the compaction step; is that correct?

A. I am giving the same response. Unless I see information otherwise, then that is expected as per good manufacturing procedures. Yes, GMP.

Q. I want the record to be clear I am asking a very specific question as to the Zydus product that comes through the compaction step. My question is whether you agree that the product that went into the Zydus roller compaction step, which is mesalamine, colloidal silicon dioxide, and magnesium stearate, whether you agree they are all blended to uniformity before compaction? Yes or no.

A. Again, following GMP, it would, it would be.

Q. Could be.

A. Following GMP, yes. Otherwise, I would have to see evidence it is not.

Q. I'd like you to go back to your deposition, tab 1, this one page 259, line 9.

Are you with me?

A. Yes.

Q. "Question: In forming that compact of mesalamine, colloidal silicon dioxide, and magnesium stearate, is it your understanding that Zydus mixes those three chemicals together before they're put through the roller compactor?

"Answer: It is not only my understanding, it is the requirement and plus BMR model you can see will tell you that. Otherwise, again, we'll have aggregation -- segregation and separation. I don't need that. I don't need quality control issues later on. So, yes, it has to be a blend. And one of the in-process control step has to be to check the blend to make sure that it is uniform and then go through compaction."

Did I read that correctly?

A. That is exactly what I said. That is correct.

Q. Do you also agree that Zydus's product contains lipophilic chemicals?

A. Yes.

Q. And one of those lipophilic chemicals is magnesium stearate, isn't it?

A. Yes.

Q. I'd like to talk a bit about magnesium stearate now, if I may, Dr. Banakar. You testified that magnesium stearate in the Zydus product is not controlled release. Do I have that right?

A. That is controlled release for the product. That is correct.

Q. It is your opinion that the magnesium stearate which is in the Zydus product before the compaction step -- in that uniform blend is what I am talking about now; right?

It is your opinion that that magnesium stearate is not controlling release at all; is that right?

A. Yes.

Q. It is also your opinion that that magnesium stearate at that point in time in the Zydus process and product, it doesn't prevent water from coming into the formulation, does it?

A. Controlled release is, you are talking about the product in the controlled release in context of the '720. That is correct.

Q. That is right. Now, would you agree that in the pharmaceutical industry, magnesium stearate is known to be hydrophobic, water insoluble, and water repellent?

A. That is correct.

Q. Now, isn't it known that magnesium stearate inhibits drug dissolution, slows it down due to its hydrophobicity?

A. You have to give me context of "slows it down." But it can have some affect, yes.

Q. Why don't we go to tab 12 in your book.

A. (Witness complies.)

Q. I'm sorry that the volume is so big.

A. Oh, sure.

Q. Tab 12.

A. Yes.

Q. Are you familiar with this?

A. Yes.
Q. This is your book; right?
A. Yes.
Q. You are the author here on the bottom, right? That's you?
A. Yes.
Q. Okay. Why don't we go to page 8-6.
A. Yes.
Q. And in the second paragraph, third line, starts: For example, magnesium stearate, a lubricant, commonly used in tablet and capsule formulations, is water-insoluble and water repellent. Its hydrophobic nature tends to retard drug dissolution by preventing contact between the solid drug and aqueous GI fluids.
Did I react that correctly?
A. Yes.
Q. That is what you stated in your book?
A. Yes.
Q. You stand by that statement, don't you?
A. Yes, but it could be taken out of context. That is what you are doing. That's fine. I still stand by this statement.
Q. And would you agree that one way to measure whether magnesium stearate is exerting a hydrophobic effect is through a water penetration test?

A. I am not an expert on water penetration test on or any kind of penetration test. But what I saw is not what I -- it was nonscientific, I think. And I did not opine on that.

Q. When you will say what I saw, you are referring to the testing by Dr. Hoag; right?

A. Yes.

Q. He did a water penetration test?

A. He called it a drop penetration test.

Q. Why don't we go to tab 11 in your book.

A. (Witness complies.)

Q. Do you have it?

A. Yes.

Q. What is this?

A. My textbook.

Q. This is your textbook. You wrote this textbook; right?

A. Yes.

Q. Okay. Why don't we go to page 253, please. 253.

A. We have the whole book?

Q. No, only a portion. Tab 11, page 253.

A. Yes.

Q. Do you have that?

A. Yes.

Q. So if we go below the line in the middle of the page,

it says: It stands to reason that the more hydrophobic the powder is, the slower the wetting and subsequent penetration of the dissolution medium across the solid surface barrier. Figure 7.1 illustrates this phenomenon which can explain the dissolution profile that results from the presence of magnesium stearate in the formulation.

Did I read that correctly?

A. Yes.

Q. Okay. If we go to the next page in your book, there is Figure 7.1; right?

A. Yes.

Q. What is shown in Figure 7.1?

Withdrawn. Let me ask it a little more directly.

The curve that I am looking at here which is in Figure 7.1, it is the uppermost curve; right? Right here (indicating).

A. Yes.

Q. And I think it has Xs. Do you know what that curve represents?

A. That, as I read it from that, the Y axis is depth of liquid penetration raised to two millimeters square as a function of timing time in seconds.

Q. And this, the formulation that this curve correlates to is one without any magnesium stearate; isn't that right?

Look right where it says.

A. Yes.

Q. Okay, you agree. And the curves down below going from top to bottom, top one has 1 percent magnesium stearate, the middle curve 2 percent, and the bottom curve 5 percent magnesium stearate; isn't that right?

A. Yes, these are very high amounts.

Q. All right. So you agree with me that in this test, when you have magnesium stearate as compared to zero magnesium stearate, the Depth of liquid penetration is much less; correct?

A. I don't know what exactly was being measured in terms of what was the basis, whether it goes to compact, whether it was a tablet, whether it was a compressed tablet, whether it was granules. We don't know that. But just looking at the pictures, I have two things that come to mind right away, without analyzing it in detail.

No. 1 is the concentrations of magnesium stearate are so humongous that we never see those high concentrations in pharmaceutical formulations that we are working with. And,

No. 2 is other factor that are the substrate which is what the measurement of liquid penetration is being done on. I don't know.

So, yes, increasing magnesium stearate amount is

showing the slope going down, which means that it is getting slanted not as steep, so that is correct. But those other coordinates I don't have.

So just taking that picture out of context and saying that, hey, look at this, the magnesium stearate is the one that is in the driver's seat, and that is the reason for this observation, that is very difficult, as you could imagine.

Q. This is a water penetration test, isn't it?

A. Yes.

Q. So your book is using a water penetration test with respect to magnesium stearate; isn't that correct? Yes or no, sir.

A. It is reporting a phenomenon which is hydrophobicity and how the hydrophobicity is linking to the solution is one of the parameters, yes.

MR. HAUG: I offer Figure 7.1.

THE COURT: Mr. Peterka.

MR. PETERKA: No objection.

THE COURT: It is admitted without objection.

MR. HAUG: Thank you.

(Figured 7.1 admitted in evidence.)

BY MR. HAUG:

Q. Dr. Banakar, isn't it known in the scientific and pharmaceutical industry that even lower percentages of

magnesium stearate can have large effects on hydrophobicity and drug dissolution? Would you agree with that statement?

A. This is a blanket statement which has to have some kind of a scope here for me to agree with that statement. But in general, you want to say, in general, do I agree. Well, I do agree any hydrophobic substance will do that, but I need a little more context to that.

Q. All right.

A. What is slowed down? What is significant? What is not? What is the hydrophobicity? What are we looking for? What is the substrate? What is the compact? What is the composition? There are a lot of stuff.

Just one statement, I cannot agree or disagree.

Q. I appreciate you didn't do a literature search on this subject; isn't that correct?

A. I know my dissolution test very well.

Q. Why don't we go to tab 15, please.

MR. HAUG: It is also PTX-629, Your Honor. I think it's tab 15 in your book.

BY THE WITNESS:

A. Yes, I am there.

Q. Do you have it?

A. Yes.

Q. Okay. It's the European Journal of Pharmaceutics and Biopharmaceutics, right?

A. European Journal, yes.
Q. Did I misspeak? I am sorry. This is a peer-reviewed journal; right?
A. Yes.
Q. Well respected?
A. No. The reason I said that, there is a European Journal of Pharmaceutics and Biopharmaceutics also.
I am just kidding. I am sorry.
Q. Thank you for the clarification. And the title is, A Comparative Study of Glycerin Fatty Acid Ester and Magnesium Stearate on the Dissolution of Acetaminophen Tablets Using the Analysis of Available Surface Area. The first author is Uchimoto. U-c-h-i-m-o-t-o.
Now, I'd like to go to the abstract and about four lines down. Four lines down.
A. Yes.
Q. It says: In the dissolution tests, a retarded dissolution of APAP was not observed with TR-FB, whereas magnesium stearate (Mg-St) which is widely used as a lubricant, retarded the dissolution.
Did I read that correctly?
A. Yes.
Q. Okay. You agree with that statement, don't you?
A. The way you read it, yes. In the context of this article, it may be true.

Q. Why don't we go to page 629.3. It is actually page 494 of the article.

A. Yes.

Q. All right. And you see the curves on the left. They are Figure 1.

A. Yes.

Q. Okay. And the curve on the top, that this is dissolution rate versus time; right?

A. A couple of things.

Q. Right now I am just asking you.

THE COURT: You have to wait ask until he asked you a question.

THE WITNESS: No, he asked you that.

THE COURT: No.

MR. HAUG: I am sorry, Your Honor.

THE COURT: Go ahead.

BY MR. HAUG:

Q. I am just asking you so we're focused on the top curve. This curve we're looking at here, Figure 1, this is a plot of dissolution rate versus time for a number of different tablets; is that correct?

A. I don't think I have seen this article right now. If you want me to, I will go through it. I can go in detail because this instant when I looked at it, there is an error in that field. So it will take time to analyze this. And

that error is so blatant on the Y axis, it cannot be weight. It has to be amount. Otherwise, the profiles are wrong.

Q. Do you recall seeing this article before?

A. Offhand, no.

Q. Down at the bottom, Figure 1, right here, it says, I am reading: Effect of lubricant concentration on the dissolution rate of APAP (100 milligrams) tablets. Figures represent (A) magnesium stearate and (B) TR-FB. Each point represents an average value of three determinations. And it goes on.

So did I read that correctly?

A. Yes, you read it correctly.

Q. And this is plotting what it says. The effect of lubricant concentration on dissolution rate. By the way, what is APAP?

A. APAP is acetaminophen.

Q. So that is what it is doing.

A. I know.

Q. This data shows lubricant concentration as a function of, or dissolution rate as a function of lubricant concentration for various different formulations of magnesium stearate in them; right?

A. With all due respect, I will refrain from commenting on this because there are errors, as I said, and I have not

looked at this. I need to look at it in more detail. If you are saying that's the figure title, you read it correctly. So off-the-cuff, I am not, I don't want to give an opinion unless you force me to.

Q. I am not forcing you to do anything.

A. Okay.

Q. Your counsel can redirect.

MR. HAUG: I offer Figure 7.1.

MR. PETERKA: No objection, Your Honor.

THE COURT: It is admitted without objection.

(Figure 7.1 admitted in evidence.)

BY MR. HAUG:

Q. Dr. Banakar, isn't it true that Zydus told the FDA that the release retardant and lubricants in its product affect both drug dissolution, both of them?

Let me try that again. It was confusing.

Isn't it true that Zydus told the FDA that both the release retardant and lubricants in its product affect drug dissolution? Do you know that?

A. I don't know that. You'd have to show me. The communication between Zydus and FDA, I don't know. I may have come across it. I don't recall that.

Q. You have no recollection sitting here now seeing any communications between Zydus and the FDA; is that your testimony?

A. I may have seen it in that paper (indicating holding hands apart), NDA -- I am sorry -- the ANDA, so they might be communicating. It is possible. If you can show me?

Q. You had your hands about a foot and-a-half or so separated. That is how much paper you were giving for the ANDA; is that right?

A. That is figurative, but it is a lot of paper.

Q. Did you read through all that paper? Did you analyze it before you gave your opinions in this case?

A. I read through most of the sections that are important. Yes, I went through a lot of material.

Q. How would you know what was important in those sections unless you read through the whole thing and found the important sections?

A. One thing for sure is the clinical section is not connected to the patent which is the substantial portion of that ANDA. So if I discard that, then it becomes this is much smaller. And then, yes, I went through the entire CMC development report, their in-house reports that were required of the development report. And then also source stipulated to the product, process, manufacturing controls, API, in-process controls, all of that.

Q. Can we turn to tab 18 in your book? It's PTX-208.

A. (Witness reviews documents.)

Q. Do you know what this is?

A. I need to get to that.
Q. Certainly.
A. Sorry.
Q. Tab 18.
A. Yes, I have it.
Q. Have you seen the quality overall summary before?
A. Yes.
Q. You have reviewed this document, didn't you?
A. Yes.
Q. This is part of the Zydus ANDA; right?
A. Yes.
Q. Okay. Let's go to page 22, please.

MR. PETERKA: Your Honor, I am going to object to this. We had a fact witness testimony on this earlier in the case. He is asking about a document that the fact witness has already testified about before.

THE COURT: Well, I'm not sure I understand your objection, Mr. Peterka. I haven't even heard the question yet.

MR. PETERKA: All right.

THE COURT: There is a document on the board. No question pending.

MR. PETERKA: I withdraw.

THE COURT: We'll hear what is happening.

MR. PETERKA: Withdraw.

BY MR. HAUG:

Q. Do you recall seeing this flow chart or depiction on page 22 of Exhibit PTX-208?

A. During the review with my -- I would have looked at it, yes.

Q. Okay. And do you see here where it says magnesium stearate and AEROSIL-200? Do you see that?

A. Yes.

Q. And there is an arrow going to lubrication; right?

A. Yes.

Q. And there is two arrows. One goes to tableting properties and another arrow goes to dissolution. Do you see that?

A. Yes.

Q. So doesn't this tell you that magnesium stearate as reported by Zydus to the FDA functions both as a lubricant as well as having an impact on dissolution?

A. No, because I think that can be an error, and I think it was covered during the presentation. This is not what I would expect, so it might be there but agree or disagree is not in my purview because the document was submitted to FDA.

Q. When you say there was an error, are you referring to prior testimony in this trial?

A. Something like that. I don't know. I don't recall where exactly, but this had come up somewhere. I don't

know.

Q. Okay. Dr. Banakar, once again, while you didn't do any literature searches regarding magnesium stearate, are you aware of any scientific articles that state that magnesium stearate forms a matrix?

A. I read a lot of stuff. I continue to read. Unless you show me something, I don't know.

Q. So sitting here right now, you don't recall seeing any publication of any kind that speaks to whether or not magnesium stearate can form a matrix. Is that your testimony?

A. If you qualify it in the context of the '720, that is a different meaning.

Q. I'd like you to go to tab 23, please.

A. Yes, I am.

Q. Okay. Are you familiar with this? This is Drug Development and Industrial Pharmacy. Do you see that?

A. Yes.

Q. Is that a respected publication?

A. Yes.

Q. You are familiar with it; right?

A. Yes, I am familiar with that.

Q. Do you use it?

A. It is a source that I go to.

Q. Peer reviewed; right?

A. Yes. Yes.

Q. The title here is Granulation Surface Area As Basis For Magnesium Stearate Concentration in Tablet Formulations, by Joseph F. Bavitz and others.

Now I'd like you to turn to page 2482, please, and underneath where it says introduction. Are you with me?

A. 2482. Yes.

Q. Okay. It says: Magnesium stearate is widely used as a lubricant in tablet formulations. It minimizes inter-particulate friction during compression and the friction between the tablet and metallic surfaces during ejection. Nevertheless, there have always been concerns with respect to lubricant levels, since excessive quantities or extended mixing times can produce a hydrophobic matrix which retards tablet disintegration and dissolution. At the other extreme is the recognition that insufficient lubricant results in tableting problems.

Did I read that correctly?

A. Yes.

Q. Do you agree with that statement?

A. I have not seen this article until right now. This is the first time I am seeing it. I would need time to look at this in context of '720.

I have already said that, yes, increasing hydrophobicity or blending excessive amounts, those are the

ones that are the keywords which tell you that, well, it is becoming, it may show some differences in dissolution. That does not mean it becomes a rate controlling matrix that is expected of this '720 patent.

Q. Dr. Banakar, a few questions again about the Zydus product and its manufacture. You agree that during the compaction step, we take the blend, the uniform blend of mesalamine, magnesium stearate, and colloidal silicon dioxide, and that is compacted into a granule; isn't that right?

A. I know what you are saying. With slight clarification. It is compacted into sheets, and then the sheets are separated into granules.

Q. Thank you. Excuse me. Thank you for that clarification. That was the picture you put up there that showed the rollers and out comes this ribbon; right?

A. Sheet or ribbon.

Q. It is the same kind of ribbon that Dr. Little testified about; right?

A. Yeah. I mean this is a very old, age old procedure.

Q. All right. But that ribbon, it is chopped up into granules, isn't it?

A. That is the function of the oscillating granulator underneath it.

Q. So the Zydus product does make granules; right?

A. Under that term, it is a granule, yes.
Q. And those granules contain mesalamine, magnesium stearate, and colloidal silicon dioxide; correct?
A. That is correct.
Q. And they contain a lot of mesalamine, right?, meaning I think you said maybe 99 percent, something like that?
A. Yes, the quantitative assessment showed 99.26 percent.
Q. And I think you had a demonstrative where you were looking at the Zydus product and do you recall the one that had all the blue dots and the four little yellow dots or whatever color they were to the right?
A. Yes.
Q. Do you remember that demonstrative?
MR. HAUG: Can we have that demonstrative? Do you know what I am talking about?
Why am I asking them. Excuse me, Your Honor.
BY MR. HAUG:
Q. It was DDX-10.21. Do you remember this one?
A. Yes.
Q. Okay. And I think I understood your testimony to be that each of those blue dots represents a milligram of mesalamine; right?
A. That is schematics.

Q. Schematic, right. And the yellow dots over here, you have got four of them, that is magnesium stearate. And your point is that there is so little magnesium stearate, 0.33 percent, that it can not act as a matrix. Is that basically your view?

A. It will not give me the matrix, unless I am shown evidence that there is a structure that is from there.

Q. And when you used the word "structure" just now, you have in mind this monolith/monolithic structure; is that right?

A. I have in mind a matrix structure.

Q. You do not have in mind an arrangement of particles in a substance or body; is that right?

A. Body of what?

Q. All right. Now, you calculated 0.33 percent magnesium stearate. How did you do that calculation?

A. If you add that together, composition of the compact, 1,209, it is absolutely wrong. It is 4 milligrams divided by 1,209 milligrams times 100.

Q. Okay. So you took the amount of magnesium stearate in milligrams and you divided it by the amount, the total tablet weight, is that right? Yes, right here (indicating). 4 divided by, is that 1,200? That is what you did, right?

A. Wait a second. Hold on a second.

No. If you look at third column, if that is

100 percent, then 3.27 of that compact weight by weight is .23.

Or, as a matter of fact, if you look at what they mention there, this is weight by weight of the total composition in terms of this compact is .27.

Q. But isn't it true what you did is you included the total weight of the mesalamine in your calculation; right?

A. That is the way weight by weight works.

Q. All right. So the .33 percent takes into account that this formulation at this point in time probably has close to whatever, well, 99.26 percent mesalamine; right?

A. Schematic is showing the significance, humongous difference between hydrophilic mesalamine and hydrophobic excipients in that compact.

Q. Isn't it true that the percentage of magnesium stearate of the total excipients in this formulation is 44 percent?

A. 44.

Q. Well, let's do the arithmetic. If I take magnesium stearate, it's 4 milligrams. I have 4 milligrams and I have 5 milligrams of colloidal silicon dioxide. That is a total of 9. If I divide 4 by 9, I think I get 44 percent.

A. If you divide 4 by 4, you get 100 percent. That is not the way it is done.

Q. I am asking whether of the total amount of

excipients, magnesium stearate constitutes approximately 40 or more percent of it?

A. Number-wise, yes, but that is misleading information in terms of what I calculate it as total composition as opposed to just the excipients.

Q. Now, when you give your opinion that there isn't enough magnesium stearate there to control release or prevent water penetration, you're basing that solely on the amount of magnesium stearate that is there in the formulation; isn't that right?

A. No, it is not right.

Q. Okay. But that is one factor, right?

A. Among others.

Q. Okay. We'll get to the other ones in a second.

So how much magnesium stearate would have to be there before you think it would prevent penetration of water? Do you know?

A. I don't think anybody will know and neither will I because magnesium stearate here is functioning as a lubricant and I cannot add 30 percent, 40 percent of and just make a magnesium stearate compact. Then it would retard significantly, but that is not the point.

Q. I'd like to ask a different question. Thank you. Am I correct that -- withdrawn.

Let me ask you this question. Do you know

whether the magnesium stearate that finds its way into the granule in the compaction step, do you know if it ever leaves the granules during further processing?

A. No, I don't know.

Q. You don't know.

A. Unless I am analytical. I do not have analytical model to see that.

Q. Were you here for the testimony of Mr. Kulkarni?

A. Yes, I was.

Q. Did you listen to it?

A. Yes, I did.

Q. I'd like you to go to tab 24 in your book.

A. (Witness complies.)

Q. Specifically, 92.

A. Excuse me?

Q. 24.

A. Yes. Page?

Q. Page 92. Sorry. Line 5.

Are you with me, Dr. Banakar?

A. Yes.

Q. Okay. This is from the testimony of Mr. Kulkarni at line 5. I'll start with the question.

"Question: After milling?

"So the colloidal silicon dioxide that was used in that first compaction process doesn't find its way out of

those granules, to be a glidant again in this later step?

"Answer: No.

"Question: And is that also true of the magnesium stearate that's used in the earlier compaction process?

"Answer: Yes."

Did I read that correctly?

A. That is his opinion.

Q. Do you have any reason to doubt the accuracy of that statement by Mr. Kulkarni?

A. I am not analyzing. This is a statement. It is a question for him.

Q. Now, am I correct that it is your opinion that magnesium stearate does not form a lipophilic matrix because it functions solely as a lubricant? Is that your opinion?

A. It functions as a lubricant, yes.

Q. So let's look back at your pharmaceutical book, testing book which is at tab 11.

Pharmaceutical Dissolution Testing, Volume 49, Drugs and the Pharmaceutical Sciences.

A. Yes. Hold on one second.

Q. Sure.

A. Yes.

Q. I'd like you to go to page 149 of your book.

A. (Witness complies.)

Q. Do you see the heading down toward the bottom, it says Lubricants?

A. Yes.

Q. Second paragraph.

A. Yes.

Q. The effects of various lubricants on the dissolution rate of salicylic acid tablets were studied by Levy and Gumtow (50). They concluded that magnesium stearate, a hydrophobic lubricant, tends to retard the dissolution rate of salicylic acid tablets, whereas sodium laurel sulfate enhances the dissolution, due to its hydrophilic character combined with surface activity, which increases the micro environment pH surrounding the weak acid and increases wetting and better solvent penetration into the tablets. Figure 5.11 illustrates the effect of lubricants on the dissolution rate of tablets.

Did I read that correctly?

A. You did.

Q. All right. You agree with that statement; right?

A. Out of context, but statement is, it shows whatever the results that these two authors have reported. So I need more information to respond to you in the context of '720. Otherwise, this statement is as is.

Q. Let's go to Figure 5.11 on the next page, page 150 of your book.

A. Yes.
Q. Up in the right-hand corner. It says Banakar. That's you, right?
A. Yes.
Q. Okay. And looking at Figure A first, do you agree with me that this is a plot of amount dissolved in milligrams versus time?
A. Yes.
Q. And what it is comparing is magnesium stearate; right?
A. Yes.
Q. And various different percentages; right? Zero percent; right?
A. Yes.
Q. Versus 0.3 percent; correct?
A. Yes.
Q. And the curve that has got the bigger sharper slope showing larger, faster dissolution, that is the one with the circles here?
A. Um-hmm.
Q. That has zero magnesium stearate in it; right?
A. Yes.
Q. And that is being compared to having 0.3 percent magnesium; right?
A. Yes.

Q. So would you agree that the dissolution is much faster when you don't have magnesium stearate in the compact as being one of the acid disks that are being testing here?

A. Let me point out where your highlight is, just behind that is salicylic acid disks. Salicylic acid is poorly soluble to begin with, and I am increasing the hydrophobicity even more, so that information you take a look at. And the objective, if I can look at this graph and look at, think about what these two authors are looking for, it is sort, it is a surfactant which is known to increase the dissolution rate. So they are taking a poorly soluble compound, not a drug, and the hydrophobic compound and a hydrophilic compound, including laurel sulfate, and seeing if I increase or decrease their amount, what effect will it have.

It has no connection to '720. But, yes, it is poorly soluble drug to deliver. This is not a formulation. So we are looking at an objective to look at what happens when I continue to increase the hydrophobicity of this disk.

So there is a lot of disparity in art, that this is telling me it is controlling or not controlling. And controlling release in context of '720 is the controlled release of the formulation, not just looking at whether just the magnesium stearate here and there without looking into the other context gives me the controlled release or not.

(Counsel confer.)

MR. HAUG: I offer Figure 5.11.

MR. PETERKA: I am going to -- in general, I don't have an issue offering the image into evidence, but Mr. Haug mischaracterized the portion that is highlighted. And I believe misled the witness. So I do have an objection to that.

THE COURT: It's not going in with the highlighting, so I hear you saying you don't object.

MR. PETERKA: No, I do. I object to the way he read the text that is highlighted.

THE COURT: Well, you will have a chance to redirect then; right?

MR. PETERKA: Yes, I guess.

THE COURT: If you wanted to object to the question and answer before, that boat is gone.

MR. PETERKA: Right.

THE COURT: You have a chance to redirect.

MR. PETERKA: All right. Then no objection.

THE COURT: It is admitted without objection.

(Figure 5.11 admitted in evidence.)

MR. HAUG: Thank you.

May I have 5, please?

BY MR. HAUG:

Q. If you go to Tab 5, Dr. Banakar.

A. (Witness complies.)
Q. Do you recognize this document?
A. Let me look at it. (Witness reviews document.)
Yes.
Q. What is it?
A. This is a Journal of Pharmacy Technology.
Q. This is a peer-reviewed publication, is it not?
A. Yes, it is.
Q. All right. And it has a date of May/June 1990. Right?
A. Yes.
Q. And if we go to the next page of the publication, it says issues in contemporary drug delivery?
A. Yes.
Q. There we are. And you are the author, are you not?
A. That is correct.
Q. All right. If we go to page 124. Table 2.
A. Yes.
Q. Okay. Table 2 says: Some primary factors influencing the rate of dissolution of dosage forms.
And then under where it says type, it says solid dosage forms (tablets, capsules, suppository).
And then in the middle column under factors, if we go down five entries, it says lubricants; right?
A. Yes.

Q. All right. And these are primary factors influencing the rate of dissolution, aren't they?

A. That is what the actuality is there.

MR. HAUG: I offer Table 2.

MR. PETERKA: No objection.

THE COURT: Admitted without objection.

(Table 2 admitted in evidence.)

BY MR. HAUG:

Q. Now, Dr. Banakar, I would like to ask you some more questions about claim construction and your opinions of infringement.

Now, the last expert report that you gave in this case was before the Court's claim construction in June or July of 2015. Isn't that right?

A. Possible. Exact date, I don't know. But, yes, you are right. It is possible.

Q. So you submitted, if I can represent the claim construction I believe was dated July 28th, 2015. And your report was filed or served at least six months before that; right? Does that sound about right?

A. If you are representing it, yes. Because I don't know the dates.

Q. Did you consider that claim construction order from the Court before you gave the opinions you gave today?

A. I don't know.

Q. I'd like you to look at PDX-14.20. This is now in your demonstrative slides. We have it up on the screen. Do you see that?

A. Yes.

Q. Now, this is a slide that we prepared; right?

A. Yes.

Q. Okay. And what we tried to do here is on the left, we have a claim limitation, and these are the various different claim limitations in the '720 patent. Right?

A. Yes.

Q. Okay. I'll represent to you that they are hopefully accurately set forth.

And then in the middle is the Court's claim construction from the Court's claim construction order back in July of 2015. Okay? Are you with me?

A. Excuse me. I didn't get that.

Q. In the middle column, I set forth the actual claim construction from the Order of the Court in its claim construction ruling.

A. Yes.

Q. Okay. And then on the right, I have construction applied in 2014 noninfringement report. That refers to your expert report in 2014. Okay?

A. Okay.

Q. And what I have highlighted in red is the differences

between your opinion in your expert report as to what you understood the claim construction to be as compared to the actual claim construction that was later issued by the Court. That is what this is about.

A. Yes.

Q. Okay. That is what we did here. So let's go to inner lipophilic matrix.

Now the Court's claim construction is "a matrix that exhibits lipophilic properties and is separate from the outer hydrophilic matrix."

In your expert report at paragraph 28, you gave this. You said this was the claim construction that you understood and that you were giving your opinion on. And you included what is in red here, you said "a matrix that exhibits lipophilic properties," and what is in red or what you have in your opinion was, "and that cannot have hydrophilic properties."

That doesn't appear in the Court's claim construction. Do you see that?

A. Yes.

Q. If you take my representation that this is accurate; okay?

A. All right.

Q. All right. And similarly for an "outer hydrophilic matrix," you did the same thing but the other way. You said

that in your view, "the outer hydrophilic matrix cannot have lipophilic properties;" right?

A. Yes.

Q. Okay. Did you ever revisit your opinions from paragraphs 28 and 29 based on that understanding of the claim construction after the Court issued its claim construction in July of 2015?

A. I don't recall. I may have --

Q. Similarly --

MR. PETERKA: He is still answering.

BY MR. HAUG:

Q. Were you finished?

A. No.

Q. Oh, I am sorry.

A. I am sorry. Maybe my voice was soft and I was going back. I am sorry.

Once -- the way I understand in writing reports is once the construction is ruled on, not comes down but ruled on by the Court, then you are to apply that. Everything else is set aside. So that is the construction I worked with afterwards. Whether I reviewed this, I don't know. I don't recall.

Q. Dr. Banakar, are you familiar -- withdrawn.

Dr. Banakar, are you aware of other litigation us that are ongoing involving the '720 patent?

A. Very cursory, yes.
Q. Very cursory?
A. Yes.
Q. Are you aware of a decision from the Federal Circuit Court of Appeals with respect to the '720 patent?
A. When you use the language Federal Court, Circuit Court of Appeals, those are foreign words to me. I don't know whether a decision is ruled on or not.
Q. Why don't we go to Tab 2 which is your supplemental expert report. Specifically, paragraph 22.

It says, paragraph 22: It is my understanding that the Federal Circuit in Shire Development, LLC v Watson Pharmaceuticals Inc. reversed the District Court's construction of the term "inner lipophilic matrix" as "a matrix including at least one lipophilic excipient, where the matrix is located within one or more substances" and also reversed the District Court's construction of the term "outer hydrophilic matrix" as "a matrix of at least one hydrophilic excipient, where the matrix is located outside the inner lipophilic matrix."

Did I read that correctly?

A. First of all, thank you very much for showing that because as I said, I don't recall. Now you showed me that, thank you very much and I stand corrected. Yes, you read it correctly.

Q. Okay. And I am not going through reading all these other paragraphs, but if you look at paragraphs 23, 24, 25, 26, 27.

A. Yes.

Q. They all start with -- almost all, 25 doesn't -- "the Federal Circuit." And then you go on and you make, you give an opinion about what the Federal Circuit said; isn't that right?

A. That is right.

Q. Did you write these paragraphs?

A. I may have.

Q. You may have?

A. Yeah. But exact wording, I don't know.

Q. Did you read any of the appeal papers that were filed in the Shire v Watson case?

A. I say the same thing. I don't recall. If you show me that, yes.

Q. Are you familiar with the recent court decision in the Shire v Watson case concerning the '720 patent?

A. As recent as?

Q. Monday of this week?

A. No.

Q. Did you see it?

A. No, no. Definitely not.

Q. Definitely not?

A. That I am for sure.

MR. HAUG: Now, I'd like, if I could have PTX-1 up again, claim 1.

BY MR. HAUG:

Q. Now, I believe Dr. Banakar, you have given the opinion that the '720 patent teaches that one must use a sufficient amount of the claimed lipophilic substances to create a matrix structure into which the active ingredient can be dispersed.

Do you agree with that statement?

A. I have stated it in my report, then yes.

Q. Does that sound right to you?

A. (Pause.)

Q. Why don't we go to Tab 2, your expert report again. Paragraph 85.

A. (Witness complies.)

Q. Are you with me?

A. Yes.

Q. Okay. Paragraph 85 in your expert report: Contrary to Dr. Sinko's opinion, the '720 patent does not teach that the presence of any amount of lipophilic material in a composition created claimed "inner lipophilic matrix." Rather, the '720 patent teaches that one must use a sufficient amount of the claimed lipophilic substance does create a matrix structure into which the active ingredient

can be dispersed. Plaintiffs' experts have presented no evidence that magnesium stearate in the compacted mesalamine forms such a structure."

Did I read that correctly?

A. That is correct.

Q. Now, I'd like you to go back. I'd like to get us back to claim 1. I have it up on the screen now.

Now, is there anything in claim 1 that talks about or is directed to what is or isn't a sufficient amount of lipophilic substances?

A. No, nothing specific. No. Nothing explicit, no.

Q. Nothing explicit. Is there something implicit or other than explicit?

A. To me, as a formulator reading this claim, if I wanted to see a structure, it will have certain amount that I can see it. And if that is not there, then I cannot say that there is a structure and therefore there is no matrix unless somebody shows me that. So the word "sufficient" is not there for structure.

Q. I understand your position on structure, but there is nothing in this claim about a sufficient amount of lipophilic material or hydrophilic material for that matter; is that correct?

A. That is correct.

Q. Now, you also gave an opinion -- withdrawn.

Do you recall earlier that you gave the opinion that the '720 patent requires two separate additions of mesalamine? Is that your view?

A. Yes.

Q. So, in other words, it is your view, your understanding of the patent that you have to have one addition of mesalamine into the inner lipophilic matrix and then another addition of mesalamine into the outer hydrophilic matrix; is that right?

A. If you read claim 1, it says that is the active ingredient is dispersed in both. So going through the claim and the specifications and reading the patent, for me, the understanding is you cannot have the drug in both unless you add it in both. You cannot just veer from that. There has to be some way that it is added in both, provided that both the structures are first added and they are separate as in the claim right now. And then also that drug is in both matrices.

Q. So am I correct to understand that as a basis for your giving your opinions, you understand there is a requirement to add mesalamine separately into the inner lipophilic matrix and the outer hydrophilic matrix? Am I correct?

A. That will be a part of the way that I would understand it, unless I am shown that how does the active

ingredient get into both of the matrices when they are identified as individual lipophilic and hydrophilic matrices.

Q. A few questions about melting point. You were here for Dr. O'Halloran; right?

A. Yes.

Q. And you actually gave some opinions based on the findings by Dr. O'Halloran; is that correct?

A. Yes.

Q. Now, Zydus' product, which is the subject of this litigation, that is not an -- the magnesium stearate in the Zydus product is not in the anhydrous form. Would you agree with me?

A. I don't know which form it is and I've not done any analysis of that.

Q. So in coming to your opinion on melting point where you gave the opinion that the Zydus magnesium stearate using its product does not meet the claim limitation of a melting point below 90, you did that without even knowing what it is, whether it's hydrate or anhydrous? Is that what you are saying?

A. The opinion I give is using a standard control test, such as a USP test. According to that, the procedures were followed correctly. I'm not a melting point expert, but I am a regulatory expert in terms of determining what is regularly available, I mean acceptable. So at this point

melting point using the -- correct. It is a standard test and that's what I opine on. I do not opine on whether it's hydrous, anhydrous, isotropic. I've heard a lot of that.

Q. I think I just heard you're not a melting point expert; right?

A. That's correct.

Q. But you still felt competent to give an opinion that Zydus does not infringe because from of the melting point limitation; right?

A. Using a standard test such as USP, which is acceptable as well as it is scientifically acceptable, on that basis, looking at what was performed by Dr. O'Halloran, it met that criteria and the melting point numbers were not below 90. That is the extent of my opinion.

Q. All right. A few questions about the outer hydrophilic matrix.

Now, you've opined in this case, I believe, that Zydus does not have an outer hydrophilic matrix as called for in the '720 patent; is that right?

A. That's correct.

Q. Am I correct that had your only argument, only argument in support of that opinion that Zydus does not have an inner -- an outer hydrophilic matrix is because, in your view, it doesn't have an inner lipophilic matrix? Isn't

that the sole basis of that opinion?

A. Along with my experience and the way the part is manufactured, the way it is structured, the way it is put together and the dissolution data, I don't see any matrix, so that's why I don't see an outer hydrophilic.

Q. Can you go to tab 2, your noninfringement report. I would like you to turn to page 55, please.

Next to where it says, Roman VI, are you with me?

A. Yes.

Q. It says, the proposed ANDA product does not contain the claimed, quote, "outer hydrophilic matrix," close quote. 149.

As explained above, it is my opinion that the proposed ANDA product does not contain the claimed quote "inner lipophilic matrix" close quote.

Because there is no inner matrix in the proposed ANDA product, it necessarily follows that there is no quote "outer matrix," close quote and the proposed ANDA product does not infringe the quote outer "hydrophilic matrix" close quote limitation of claim 1 as well.

Did I read that correctly?

A. Yes, you did.

Q. All right. And my question is, isn't it true that this is the only opinion you gave in your expert report

about why the Zydus product does not have an outer hydrophilic matrix?

A. In the words, it is my opinion. That opinion includes all the other information that I just told you, so that was not recited as correct, but in your context, yes, there's only one paragraph which talks about it.

Q. I would like to put up -- one second.

MR. HAUG: Do we have a slide? I'm sorry. PDX-9, which would be the slides for Dr. Sinko.

Tab 39. Let's do it this way. Tab 39 in your book. Okay. Are you with me?

A. No, not yet.

Q. Not yet. Sorry.

A. Okay.

MR. PETERKA: Is this going into evidence? I object.

MR. HAUG: I have not moved it into evidence.

MR. PETERKA: All right.

MR. GAERTNER: May I speak, Your Honor? I don't want to have two lawyers.

We had an agreement with counsel at the initial -- from the original part of the case when we first showed up in front of Judge Jordan.

MR. HAUG: It is what it says.

THE COURT: Whoa, whoa, whoa. Do not talk to

each other. You've got to talk to me.

MR. GAERTNER: I apologize. I apologize.

MR. PETERKA: Your Honor, I misremembered. I thought he represented to me they are Dr. Sinko's slides. They are not. We did have an agreement at the claim construction hearing not to be used for any purpose in the case later on, and that's on the record.

MR. HAUG: May I speak --

THE COURT: Sure.

MR. HAUG: -- to that?

I don't actually remember the agreement that way, but I will just simply withdraw that question.

THE COURT: That's fine. And -- good enough.

MR. HAUG: May I have just --

THE COURT: You still have a minute yes.

(Pause while counsel conferred.)

BY MR. HAUG:

Q. I have a question about, remember that demonstrative you had with all the blue dots, the four yellow dots?

A. Yes.

Q. All right. And you had -- you were showing what you believed to be the percentage of magnesium stearate compared to mesalamine; right? Correct? Do you have it?

A. Can you tell me where it is, please?

Q. Sure. I think it's DDX-10.21.

A. Yes.
Q. Okay. Now, do you know what the molecular weight of mesalamine is?
A. Not offhand.
Q. Do you know what the molecular weight of magnesium stearate is?
A. No.
Q. Do you know how many carbon atoms there are in magnesium stearate?
A. A lot, because it has the long chain.
Q. A lot more than mesalamine; right?
A. Can you bring up the picture?
Q. Sure. DDX-10.21.
A. Yes. So as I referred to it numerous times in the schematic, one unit milligram is one dot. I never said it was certain molecular weight or number of carbon atoms. It isn't scaled to the molecular weight.
Q. Magnesium stearate is a much bigger molecule than mesalamine; right?
A. I don't know.
Q. You don't know. Okay.
MR. HAUG: Could we go to DDX-10.26, please.
BY MR. HAUG:
Q. Do you recall this slide? You were talking about the prosecution history of the '720 patent.

Do you remember that?

A. Yes.

Q. This slide, DDX-10.26.

A. Yes, I do.

Q. Okay. And on the left, this is a picture taken from the prosecution history. And do you see where it says, drug in polymer matrix, and it has got, like an arrow maybe pointing to a dot?

Do I have that right?

A. Yes.

Q. So all of those dots are supposed to be drug; is that right?

A. That is correct.

Q. Well, the mesalamine in the Zydus formulation, it would never look like that, would it?

A. That's exactly what I'm expecting if matrix is the way it's defined by the Court.

Q. And then on the right disclosure, where it says disclosure, down below it says, drug in polymer matrix.

Are you with me?

A. Yes.

Q. And then underneath it says microparticle, a monolithic system of approximately one to several, 100 micrometers in diameter; right?

A. Yes.

Q. Approximately one micron is very small, isn't it?
A. Yes.
Q. And how can this be a structure in your expert opinion based on your understanding of a structure as it is required by the patent?
A. Microparticles, that that is a microparticle. Okay. So now if you can imagine, if I have a polymer and I take the drug, blend it with that polymer, compress it, that drug might be -- I might have a particle size of one micron, a hundred microns, and those are distributed in that polymer matrix. And then over the next -- next slide, I show that the drug leaves this out and what is left behind, that is the structure.
Q. And the mesalamine which is used in the patent examples --
A. Yes.
Q. -- switching now back to the patent; right? The '720 patent has how many examples? Do you know?
A. I can look at it.
Q. Do you know how many without looking at it?
A. Five.
Q. Five. Okay.
And do you know if the mesalamine in the patent examples would look anything like either of the pictures that are shown on your slide, DDX-10.26, which on the left

comes from DTX-2, and on the right from DTX-13?

A. That is the burden that I -- you have to show me, because this is how the patent also said the matrix would be formed.

Q. You say the patent says it has to be this way because these, whatever these references are, they were provided to the Patent Examiner during the prosecution of the patent; is that right?

A. That is my understanding.

Q. So it was your understanding that because literature references or publications were provided to the Patent Office, that that means that it's a limitation, right, on what the patent covers? Is that what you are saying?

A. I don't know the legal -- meaning of the word "limitation," but what I am expecting is, matrix as also defined by the Court has to have a structure, and that structure is what I'm looking for, which is represented in this, and that's exactly what the patentees did to the Patent Office to get them separated out from the prior art. So forget about that. But that is exactly what they said, and that is my opinion.

I don't know the word, legal word, an understanding of the limitation and how it is to be interpreted, but that's exactly what I'm expecting and I don't see that here in evidence. If you show me that, then

I will take a look at it and evaluate it.

MR. HAUG: Thank you. No further questions.

THE COURT: All right. Thank you, Mr. Haug.

Mr. Peterka, any redirect?

MR. PETERKA: Yes. Just one thing.

THE COURT: You are on the clock.

MR. PETERKA: Hello again, Your Honor.

REDIRECT EXAMINATION

BY MR. PETERKA:

Q. Dr. Banakar, I just want to walk through a few things that Mr. Haug just covered with you if you don't mind.

A. Yes.

Q. I would like to have you turn to tab 11 in your binder that Mr. Haug gave you.

MR. PETERKA: Does this work?

THE COURT: Yes, the Elmo should work.

MR. PETERKA: You know what, Your Honor. I have a slight problem. I wrote on my copy, the part I want to show the witness. Could I perhaps borrow Dr. Banakar's copies of the exhibit to put on the Elmo? I would like to show him something.

THE COURT: If you would like to do that, you can freely approach.

MR. PETERKA: Okay.

BY MR. PETERKA:

Q. Mr. Haug showed you this article, or this table earlier from, I think it's from your book; right?

A. Yes.

Q. I believe he asked you if -- on Figure 11, plot 11 in the legend there under, after the word salicylic acid disks, open parentheses, (A) close parentheses (E)?

Do you see that?

A. Pardon?

Q. All right. Do you see the (A) after salicylic disk in Figure 511?

A. Yes.

Q. It says (A). Then there's an open circle, three percent?

A. Yes.

Q. Then there's magnesium stearate and semicolon, closed circle, no magnesium stearate?

A. Yes.

Q. I believe I heard Mr. Haug refer to that 0.3 percent magnesium stearate. I just want to -- is that how you view that?

A. No. Both of the legends, that is three percent with this and zero percent.

Q. Okay. Thank you.

And this is --

THE COURT: Figure 5.11?

MR. PETERKA: Yes.

THE COURT: It was admitted as a plaintiffs' exhibit.

MR. PETERKA: I don't know if it was admitted.

THE COURT: Go ahead.

MR. PETERKA: It was tab 11 in Dr. Banakar's binder. It was admitted as 5.11.

BY MR. PETERKA:

Q. If you could turn to tab 23 in your binder that Mr. Haug gave you, and if you could go to page 2485. I'm sorry. 2482.

A. Yes.

Q. And Mr. Haug showed you this, this reference earlier. I just want you to -- you've read in that first paragraph there it starts halfway down, it starts, nevertheless, there have always been?

A. Yes.

Q. Can you read that?

A. Nevertheless, there have been -- there have always been concerns with respect to lubricant level since excessive quantities are standard mixing times, tablet disintegration.

Q. And if you turn to Table 1 in this reference, 2485, do you see there's a formulation there for the mannitol formulation?

A. Yes.
Q. Actually, I withdraw that.
Is there any evidence of excessive quantities or extended mixing times for a lubricant in the Zydus ANDA product?
A. No.
Q. Can you turn to tab 15 in your binder.
A. Which one?
Q. The first binder, the one Mr. Haug gave you.
A. Yes.
Q. This is the Uchimoto reference?
A. Yes.
Q. If you turn to page 494, there's a Figure 1 there.
A. Yes.
Q. And what is the amount of, what are the amounts of magnesium stearate that are used in the formulations that are tested in that figure?
A. From .1 to 3 percent.
Q. I see.
Now, at .1, for Figure -- in Figure 1 under part A, the top one there.
A. Yes.
Q. Do you see there's a concentration of 0.1 percent?
A. Yes.
Q. And the dissolution rate is almost instantaneous;

right?
A. Yes. You do it rapidly.
Q. Okay. Now, what about at the .5 percent? Would you consider that to be immediate release?
A. Yes.
Q. All right. And there's nothing on this, in this figure showing a magnesium stearate content of less than .5 percent; is that correct?
A. That is correct.
Q. And there's nothing here showing a magnesium content, magnesium stearate concentration of .33 percent; is that correct?
A. That is correct.
Q. Did Mr. Haug show you any reference that studied the effect of magnesium stearate or that showed an effect on dissolution from an amount of magnesium stearate that was less than 0.5 percent?
A. No. There was three percent and high, pretty high.
MR. PETERKA: Can I have -- I guess we've got to turn this off.
Can I have Dr. Banakar's slide? There was a slide towards the beginning with the claim constructions on it.
BY MR. PETERKA:
Q. Just to be clear, this is DDX 10.6, Dr. Banakar.

A. Yes.
Q. In your slide deck.
This lists the claim construction from the Court as you're aware; is that correct?
A. Basically.
Q. These are the claim constructions that you applied when forming your opinions that you gave today; is that correct?
A. That is correct.
MR. PETERKA: No further questions.
THE COURT: All right. You may step down.
(Witness excused.)
THE COURT: Do you have any other witnesses?
MR. GAERTNER: No, Your Honor. The defense rests.
THE COURT: Plaintiff? Mr. Haug, do you have any witnesses in a rebuttal case?
MR. HAUG: No witnesses. Plaintiff rests.
THE COURT: All right. Both sides rest. Any applications?
MR. GAERTNER: Your Honor, on behalf of the defendants, we renew our motion for judgment under Federal Rule of Civil Procedure 52 for the same reasons we did at the close of plaintiffs' case. I would be happy to argue those for you again. It's up to you how you would like to

handle it.

THE COURT: No. I remember what you said.

Mr. Haug, your response?

MR. HAUG: I guess I would say the same. I certainly repeat everything I said, plus we've had additional testimony entered into the record through cross-examination of these witnesses, which I think go to our proofs in the case showing where there's a lipophilic matrix, the function of magnesium stearate is in that inner lipophilic matrix.

We have additional evidence about the dissolution. We have additional evidence about the outer hydrophilic matrix, its separateness. And, of course, we have a lot of evidence now in the record about melting point. And it's clearly a question of fact at this point, Your Honor, and I think that to grant any motion at this point would be -- we certainly pro oppose that, because I think there are way too many factual questions in the record.

THE COURT: All right. Thank you, Mr. Haug.

I will give you the last word if you want it, Mr. Gaertner.

MR. GAERTNER: No. I'm fine, Your Honor.

THE COURT: All right. Well, again, I will deny your motion without prejudice. I will look forward to

receiving the parties' post-trial submissions.

Let's take a moment at this point. Subject to giving both parties an opportunity to confer with the courtroom deputy to make sure that the exhibits that were tendered, intended to be tendered, in fact, are noted as in the record, we'll consider the record closed at this juncture.

Mr. Haug?

MR. HAUG: Yes. Sorry. Early on, Mr. Kulkarni, when he testified, there were a couple of lines out of order in the copies we gave the Court and we asked you to correct that, which we did, so I will hand that up.

THE COURT: That's fine. Why don't you go ahead and give the corrected copies to the deputy afterwards. All right?

MR. HAUG: Very good. Thank you.

THE COURT: Well, look. I want to say a couple things real quickly.

First, I appreciate the very thorough, professional job that both sides did here, and I hope representatives from your clients, that the parties are present in the courtroom to hear me compliment, you and compliment both sides highly for the work that was done.

Somebody is going to end up unhappy. That's just the nature of the business we're in. Right? But it

won't be for lack of trying. It won't be for lack of significant and highly skilled work on the part of the litigation teams.

So I don't say that lightly. I compliment you both. I appreciate the professionalism with which you treated the various disputes in that arose, minimized the need for Court involvement, worked problems out where you could, got me involved only when you had to. You're a credit to your firms and to the clients you serve.

And thanks for bringing it in on time so we did not have to have a problem with that.

Let's talk logistics for just a moment. Okay? Since there is no invalidity case at this point, the burden is squarely on the plaintiffs. I will give the plaintiff an opening and a reply, the defendants an answer in terms of briefing.

Both sides can submit -- I hope I don't regret my doing this, in addition to that, the argument, which I expect to see in the briefing, you can cross submit proposed findings of fact and conclusions of law, and cross-submit replies in which you take those on.

Do you understand what I'm getting at? Okay. So I'm talking about two separate sets of submissions, one set being the briefing, the other set being the conclusions of law and proposed findings of fact in which each side has

an opportunity to respond to the other side.

I would like to have this wrapped up from your end, that is in my lap, within six to seven weeks. That's given the responsibility I'm going to have to get this done and done by September. Given the responsibilities I have, I figure it's not untoward for me to ask for three months, so I will give you guys close to two months, because there's one of me -- that's not fair to say. I've got a great clerk working with me on the case, so he he's worth at least two or three of me, but it's still nothing next to how many folks you've got to work on this.

So if that seems like a short time, I'm going to be working on a short fuse, too, and I'm confident your clients would like to have an answer to this an way.

So with those time parameters in mind, I will ask the parties to get together. You've got daily copy, so you are not waiting for the transcripts. I will ask the parties to get together and discuss a reasonable schedule to get this all submitted so that I can start working on it. Okay?

MR. GAERTNER: Yes.

THE COURT: And when do you think I could expect to hear from you about an agreed upon schedule?

MR. HAUG: We will do it tomorrow.

MR. GAERTNER: Some of us may be in transit

tomorrow because we have -- Monday or Tuesday, Your Honor. I think a couple days.

THE COURT: All right. No later than Tuesday get back to me, because I want to write "So Ordered" on a piece of paper so that we all know what we're talking about. Okay?

Yes, Mr. Gaertner?

MR. GAERTNER: Page limits, Your Honor, did you want us to keep in mind?

THE COURT: Local rule page numbers for the briefing. All right? And on the findings of fact and conclusions of law, the answer is, no, there are no page limits, but I hope you'll exercise good judgment. All right?

MR. GAERTNER: Your Honor, can we ask for a few more pages than the local rules?

THE COURT: You would have to make your case to me. All right? You are going to have lots of paper with those findings of fact and conclusions of law, but I will listen to you.

If you think -- you confer with each other. Here's what I don't want. I don't want to hear from you that on top of giving you the opportunity to submit all the findings of fact and conclusions of law that you want and a response to each other on that, that you also think you need

an enormous amount of briefing to support it, because I think you are going to be okay. But if you want to push down a little bit, you can talk to the other Zydus and talk to me. Okay?

MR. GAERTNER: Thank you.

THE COURT: All right. Great job, you all. Thanks very much. We stand in recess.

MR. GAERTNER: Thank you.

(Bench trial proceedings ended at 4:42 p.m.)

I hereby certify the foregoing is a true and accurate transcript from my stenographic notes in the proceeding.

/s/ Brian P. Gaffigan
Official Court Reporter
U.S. District Court